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Neurocirculatory Asthenia, Anxiety and Neurosis 711
Henry H. W. Miles and Stanley Cobb

Control of Inoperable Oral Cancer with Massive Roentgen Therapy 719
George White and William R. Christensen

Suicidal Dilantin (Sodium Diphenylhydantoin) Poisoning 723
Jerome B. Tichner and Charles D. Enselberg

Roentgen Therapy in Acne. 726
G. Marshall Crawford, Ralph H. Luikart, Jr., and Robert F. Tilley

Obituary 748
Massachusetts Medical Society 748
Massachusetts Department of Public Health . 749
Miscellany. 750

Medical Progress: Cerebral Palsy. 728
(To be concluded)
Eric Denhoff, Victor N. Smirnoff and Raymond H. Holden

Case Records of the Massachusetts General Hospital 736

Editorials:
Abuse of Transfusion Therapy 745
Preprofessional Education for Medicine 746
Old Books: New Libraries. 747
Crime Detection at Harvard 747

Correspondence. 750
Books Received 750
Notices 752

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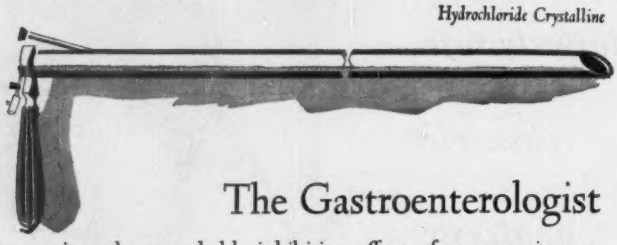

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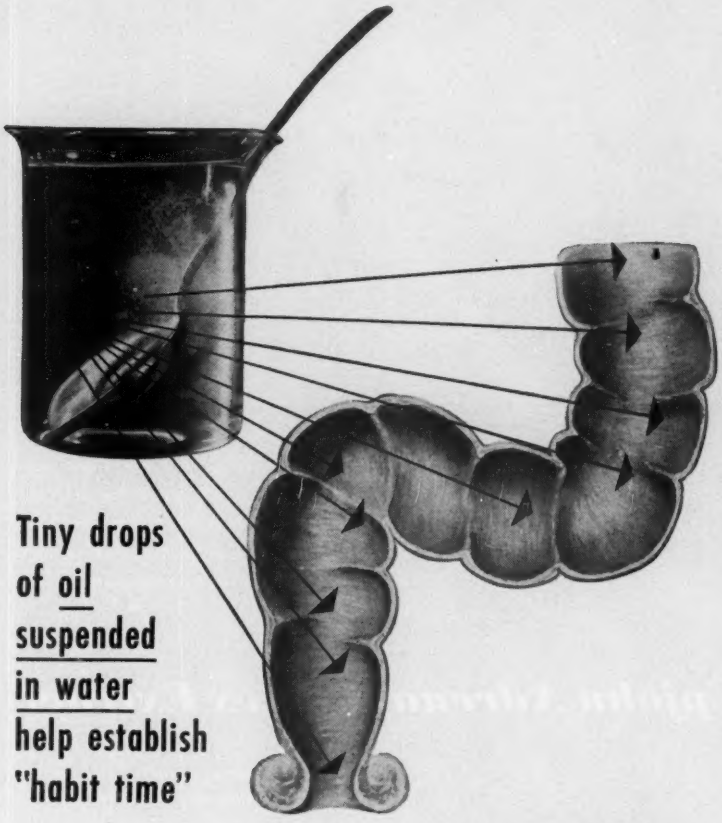

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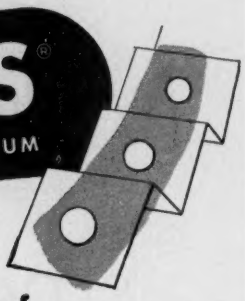

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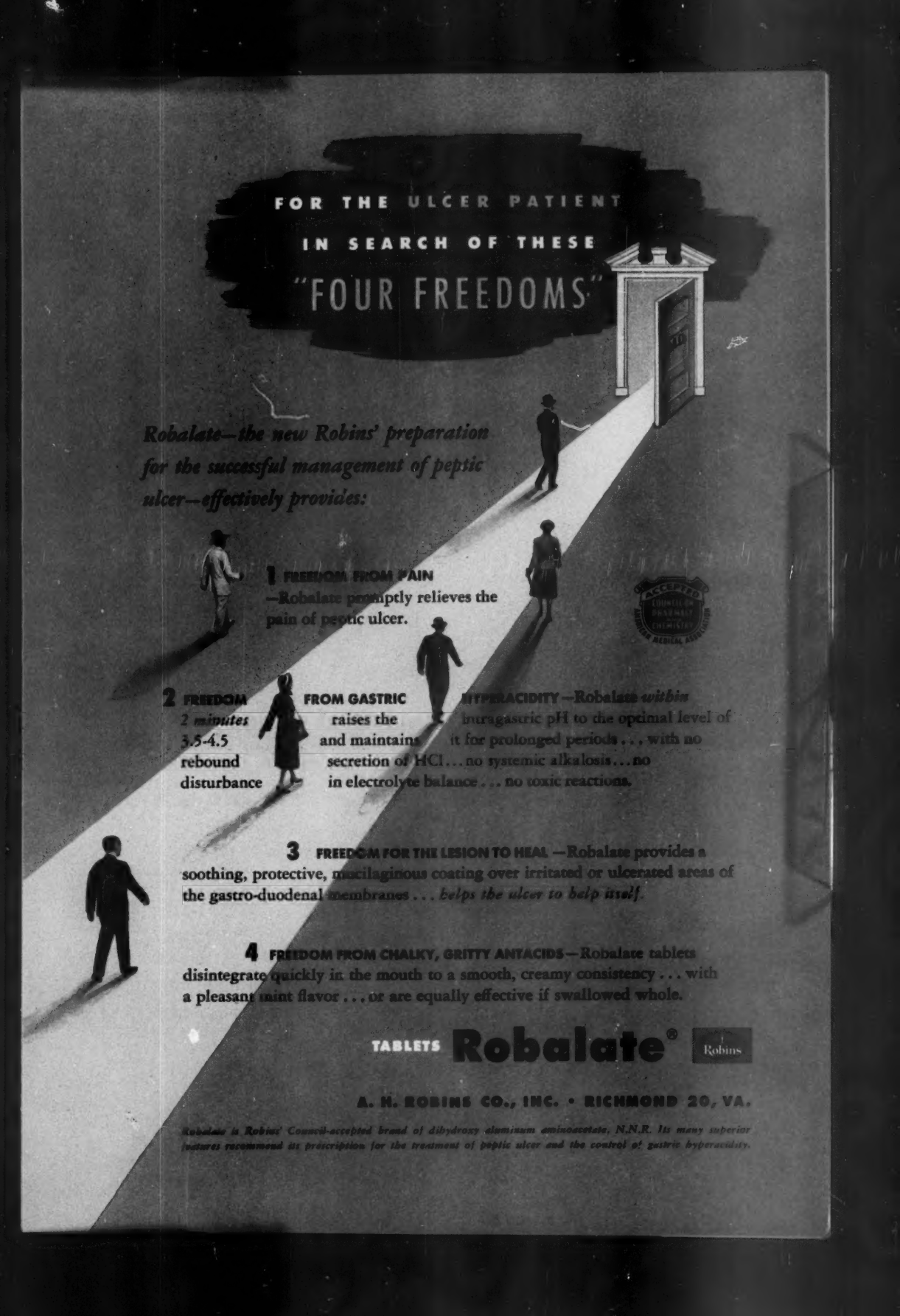
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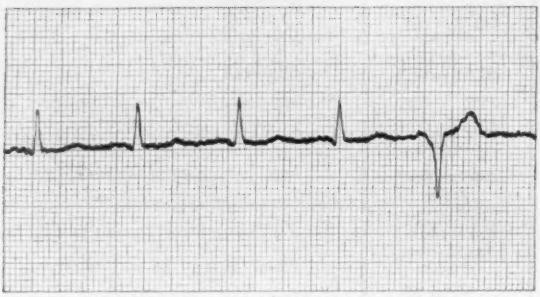
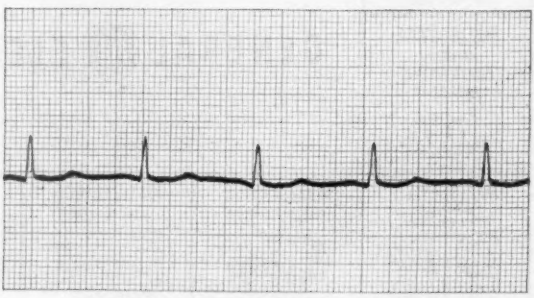


Lead I. Control tracing, ventricular premature contraction.



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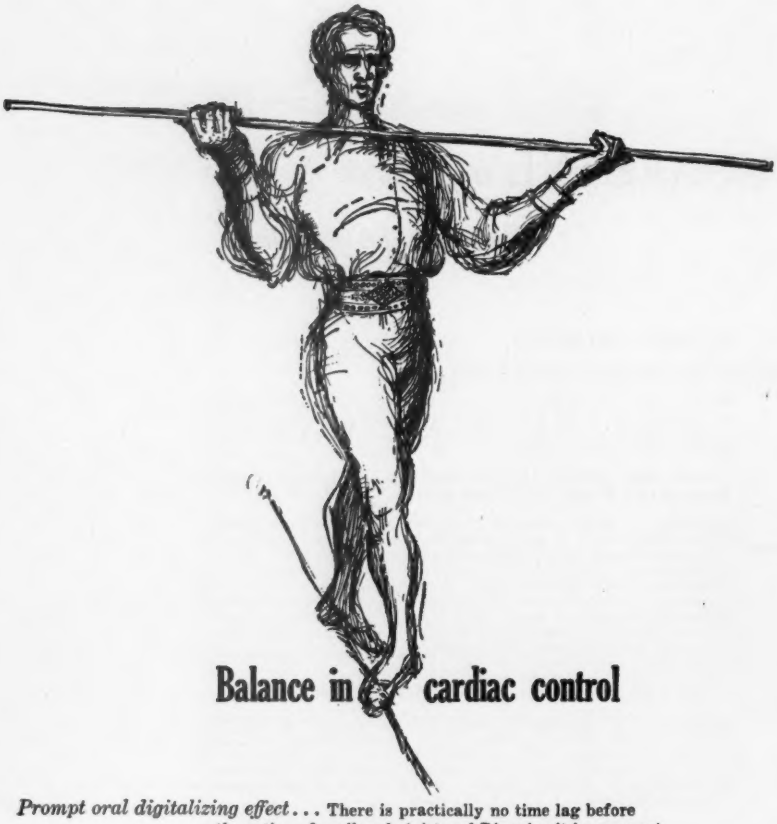

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1. Schaaf, R. S., Hurst, J. W., and Williams C.: Med. Clin. North America (Mass. Gen. Hosp. No.) p. 1255 (Sept.) 1949.

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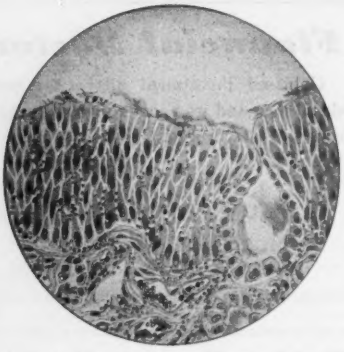

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Volume 245 NOVEMBER 8, 1951 Number 19

NEUROCIRCULATORY ASTHENIA, ANXIETY AND NEUROSIS*

HENRY H. W. MILES, M.D.,† AND STANLEY COBB, M.D.‡

BOSTON

NEUROCIRCULATORY ASTHENIA VERSUS ANXIETY NEUROSIS

THE constellation of symptoms called *neurocirculatory asthenia* (NCA) is frequently encountered in medical practice, but despite its prevalence it is still a source of much argument and confusion. Extensive clinical and laboratory investigations have resulted in data that are inconsistent and controversial. Some recent reports[1-4] have stressed the opinion that NCA is identical with "anxiety neurosis."§ We believe this to be an unsound postulate and will attempt in the present paper to clarify our views. The patients classified by Wheeler and his co-workers[3] as having "neurocirculatory asthenia (effort syndrome, anxiety neurosis)" are grouped together merely on the basis of common symptoms. The authors define their syndrome as " . . . a state of ill health characterized by a large number of symptoms, including breathlessness, palpitation, chest pain, nervousness, fatigue, headache, dizziness, sighing, attacks or spells, apprehension, trembling and discomfort in crowded places, in the absence of other disease which might reasonably account for these symptoms." Their specific criteria for making the diagnosis are "breathing trouble and symptoms from two of the following three groups: (1) palpitation or chest pain; (2) nervousness, dizziness, faintness, attacks or spells; and (3) feelings of fatigue or tiredness or limitation of activity."

This definition does closely resemble that given for anxiety neurosis, and to prevent misunderstanding let us emphasize now that it is not the *label* to which we object but rather the concept of disease¶ that is implicit in a purely descriptive diagnosis. The paper by Cohen, White and Johnson[1] gives the impression that they believe that all patients with the NCA syndrome have the same illness, for in the conclusion they state: "The cause, anatomic changes and specific treatment are obscure." This belief may not be shared by the majority of cardiologists; for example, Friedberg[5] says of NCA: "Despite the distinctive titles given to this syndrome it is not a nosological entity. It is nothing more than a moiety of the more general picture of psychoneurosis, which, in the cases under discussion, chances to assume entirely or predominantly the garb of cardiac or circulatory symptoms."

Our thesis is that if defined *only* by a list of symptoms, neither "NCA" nor "anxiety neurosis" is a useful nosologic or heuristic entity. In the group of illnesses that psychiatrists subsume under the generic term "psychoneurosis" or "neurosis" there are many that have enough of the symptoms on Wheeler's list to be designated as NCA. However, they are not identical disorders. It is readily admitted that our present systems of classification of the neuroses are unsatisfactory, whether based on symptoms, psychopathologic structure or both, and that the various diagnostic syndromes are not clear-cut entities. Nevertheless, in working toward a dynamic understanding of any illness the multiplicity of etiologic factors should be emphasized. These may be numerous and can be tentatively summarized under four headings: *histogenic*, or due to lesions; *genogenic*, or inherited; *chemogenic*, or related to variations in body chemistry; and *psychogenic*, or associated with emotional conflicts and disturbed interpersonal relations.[6] At present we know nothing about histogenesis in "NCA" or "neurosis," very little about genogenesis or chemogenesis and a good deal about psychogenesis.

We cannot assess accurately the constitutional factors,|| but there is suggestive evidence that some patients who might be diagnosed by their symptoms as having NCA or anxiety neurosis do have a physiologic deficit,—either hereditary or due to as yet poorly understood biochemical abnormalities,

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§A widely used descriptive definition of anxiety neurosis is that approved by the American Psychiatric Association: "Cases which show more or less continuous diffuse anxiety and apprehensive expectation, with paroxysmal exacerbations associated with physiological signs of fear, palpitation, dyspnea, nausea, diarrhea, are to be classified here. Emotional tension is apt to be high, and irritability and intense self-preoccupation may be prominent, particularly during episodes. The diagnosis should not be made until all other more clearly defined types showing anxiety as a symptom have been excluded."

¶"Disease" is here defined broadly as a condition of impaired health resulting from disturbances in the equilibrium of a person reacting as a whole to external or internal stimuli.

||Here defined as hereditary and developmental abnormalities.

—that renders them unable to tolerate physical exertion to the same extent as "normal" persons. If this were established, one could classify patients according to the predominant discernible factors: "somatic" (genogenic and chemogenic) at one end of the scale and "neurotic" (psychogenic) at the other. Since most cases probably have a mixture of causative factors in varying proportions, it seems more accurate to think of the differentiation in terms of a frequency-distribution curve with a few relatively straight "somatic" cases at one end and a number of clearly "neurotic" cases at the other. The majority are mixtures and fall somewhere in between, according to the proportions of the factors involved. We believe that this sort of division, rather than a clear-cut dichotomy, is of fundamental importance and is still not sufficiently appreciated in medical thinking and teaching. One still encounters many instances of adherence to the fallacious concept of polar antitheses—for example, in regarding an illness as *either* inherited *or* acquired or as *either* somatic *or* psychologic.

The following two cases illustrate the two types of illness according to the predominant etiologic factor (the opposite ends of the distribution curve).

Case Reports

Case 1. Mr. S., a 21-year-old single man, had had weakness and palpitation for 9 years. His medical history was not contributory except for a "serious illness with high fever," which he was said to have had when 1 year old.

At the age of 12 he began having bad dreams and complained of spells of palpitation, usually occurring in school. He became nervous and so much concerned about the state of his health that he was taken out of school for 3 months. The family physician was unable to find any evidence of a medical disease. At the age of 14, when he took a part-time job after school, he discovered that the exertion tired him very quickly and made him breathless. Bouts of palpitation recurred, and he was told by the family doctor that he had a "nervous heart." Any strenuous exertion led to palpitation, breathlessness and weakness. He was convinced that something was wrong with his heart and was preoccupied with his various symptoms, which also included shakiness, precordial pain, "shivery spells" and occasional indigestion.

Marked intolerance to exercise had been noted only since the patient was 14. Whether or not this had manifested itself at an earlier age was difficult to determine. As a child he had played normally with other children, but as he grew older he had not participated in team sports or organized athletics.

Physical examination and laboratory studies were within normal limits. It was recorded that the extremities were cool and sweaty and that the pulse was unstable and the blood pressure was 106/68. The chest x-ray film was normal, but the comment was added that the heart appeared small.

During a long period of psychotherapy in the hospital and later in the out-patient department a great deal of information was accumulated about the patient's interpersonal relations and conflicts. He spoke of his anxiety and guilt feelings concerning masturbation and his marked inhibition of heterosexual drives. He was aware that his symptoms were related not only to exertion but also to situations in which he was exposed to excitement, social anxiety and competition. Gradually the patient developed a warm regard for the therapist and derived much reassurance from the interviews. Symptomatically he improved considerably. The main emphasis in the treatment was on a physiologic explanation of the symptoms and positive reassurance that there was no heart disease.

Twelve years later, when he was 33, the patient was seen for a follow-up evaluation in a series of interviews. He had maintained a symptomatic improvement but only at the expense of a restricted life. His fear of failure was so strong that he had taken a job that was not commensurate with his ambition or his ability. He also had fears about his potency and continued to masturbate with feelings of self-disgust rather than face the test of a heterosexual relation. He believed that exercise might "build him up" but found that no matter how often he joined calisthenics classes or exercised in the gymnasium he could tolerate only a moderate amount of exertion before becoming breathless and apprehensive about the pounding of his heart.

Comment: The history and course of the illness suggest that this man had an actual physiologic intolerance for exercise. There were, of course, many neurotic problems, which the patient was able to solve partially but not effectively by a restricted life. This case represents the "somatic" type (constitutional factors predominate), but it has not been our experience that one can find a pure example; psychologic factors are always present in some degree.*

Case 2. Mr. L., a 29-year-old married man, said that he had been ill for about 15 months. His illness began rather suddenly with "burning sensations" in the epigastrium, nervousness, "blood rushing to his head," muscular weakness and chronic fatigue. Medical examination, including a gastrointestinal series, revealed no evidence of disease. The patient was subsequently treated briefly in a sanatorium and by several physicians with various injections, diets, and tonics. He felt worse, had to quit work and continued to have many disabling symptoms, including anxiety attacks, "choking" (somewhat relieved by getting out into the fresh air), sighing, palpitation, weakness, fears and fatigue. During the illness he lost about 15 pounds. For 3 years (since 1 month before his marriage) he had had recurrent episodes of urticaria, sometimes coincident with the anxiety attacks.

Prior to the onset of the present illness the patient had considered himself healthy. He had worked regularly and efficiently, and although not athletic he had had plenty of energy.

Physical examination revealed nothing of significance except a slight tremor of the hands and sweaty palms. The blood pressure was 120/60; laboratory data, including electrocardiograms and chest x-ray films, were within normal limits.

Interviews were carried on four or five times a week during the patient's 2½-month stay in the Psychiatric Ward. He was first encouraged to discuss his symptoms and his current life situation. It soon became clear that marital conflicts were important, despite his early protestations that all was well. The onset of his illness was found to coincide with a stress situation that had a number of special meanings for the patient. Symptoms began when he incurred debts and asked his wife to get a job so that they could pay off the bills. She refused, saying that she had not married him with the intention of going to work. This was a threat to his self-confidence, and he found himself unable to discuss his feelings with her. She also made him feel inadequate sexually, as she wanted him to make love more aggressively than he was able. In the interviews he gradually expressed much hostility toward his wife, with a marked emotional reaction. This was accompanied by a temporary increase in anxiety, after which he felt much better.

The patient later discussed his relations to men — especially a strong attachment to his father. (His mother had died when he was a boy.) He had painful feelings of inferiority with respect to his older brothers, and at this point needed active reassurance that the therapist was really interested in him. Finally he was able to admit strong feelings of guilt concerning adolescent homosexual experiences involving an uncle and one of his older brothers. The therapist showed interest and a kindly attitude but made no attempt at interpretation of

*One cannot hope to "prove" the existence of a constitutional intolerance to exercise, since the question invariably arises whether psychogenic factors originating in early childhood might not result in such inhibition of activity that the patient never *learns* to tolerate effort.

the passive homosexual acts. Symptomatically, the patient improved steadily. He gained 10 pounds, lost his anxiety attacks and was discharged much improved.

Nine years later, when seen for a follow-up evaluation, he was in good health. He had divorced his wife and had gone back to live with his father and a married sister. We interpret his improvement as being related to several things. Ventilation of the emotional conflicts and the development of a warm and secure doctor-patient relation probably contributed most to the immediate symptomatic relief. The maintenance of this improvement can be understood dynamically on the basis of the dissolution of the marriage (which relieved him of much stress) and a return to a relation with his father in which the unconscious passive attachment could be gratified without feelings of guilt.

Comment: This man, in contrast to the first patient, had no evidence of exercise intolerance until the onset of symptoms in a setting that was emotionally stressful to him. It should be emphasized that the conflicts were largely *unconscious* (that is, the patient was not aware of their significance), as the understanding of a neurosis depends on the recognition of unconscious processes. This case is a good example of the psychogenic type of "NCA syndrome."

We think that the evidence shown in these cases is clear enough to warrant a distinction between symptoms of breathlessness, fatigue, palpitation and so forth due chiefly to a *physiologic deficit* and symptoms related to *psychologic conflicts*. Usually in clinical practice the correlation between symptoms and emotional conflicts is much more apparent than is any physiologic abnormality. In the majority of cases no distinction can be made; if the patient is examined by a cardiologist or internist the diagnosis is "NCA"; if by a psychiatrist, "neurosis." We suggest that in those few cases that *can* be differentiated separate diagnostic labels should be available, perhaps using "NCA" or "effort syndrome" to designate those having evidence of a physiologic deficit with little or no overt anxiety.

Although many patients diagnosed as having NCA or anxiety neurosis have the same illness, there may be a certain "natural selection" in these two groups. The patient whose complaints are primarily referable to the cardiovascular system is apt to go to a medical doctor, whereas the one whose symptoms are predominantly diffuse anxiety, irrational fears, depression or nervousness may consult (or be referred to) a psychiatrist.

Figure 1 shows a comparison of the frequency of some of the more common symptoms in 60 cases diagnosed as NCA[3] and 50 diagnosed as anxiety neurosis.[7] In the former group there is a greater incidence of effort trouble, sighing, breathlessness, smothering, dizziness, paresthesias, chest pain, pain radiating to the left arm and vascular throbbing. In the anxiety group one sees more bad dreams, sweating, chronic fatigue, depression, apprehensiveness, shaking or trembling and nervousness. In the latter group acute anxiety attacks were present in 86 per cent, but as this symptom was not recorded for the patients with NCA no comparison can be made. In another group of patients with NCA studied by Cohen, White and Johnson,[1] "attacks" (presumably anxiety attacks) were reported in 70 per cent of the chronic cases and 72 per cent of the acute cases.

One cannot be sure that the differences in this "symptomatic profile" of the two groups are significant, but certain points support our thesis. The NCA group had a higher incidence of effort trouble than did the anxiety group. On the other hand, chronic fatigue (unrelated to effort) appeared more often in the patients diagnosed as having

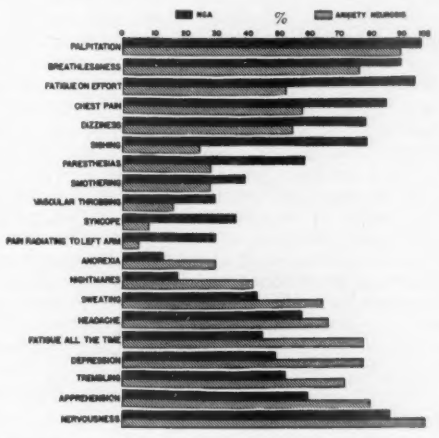

FIGURE 1. *Incidence of Symptoms (Expressed as Percentages) in 60 Patients with NCA and 50 Patients with Anxiety Neurosis. "Fatigue on effort" is synonymous with "effort trouble" or "tires easily." "Fatigue all the time" means chronic fatigue unrelated to effort. "Nightmares" is a term used for "bad dreams" or "frightening dreams." "Depression" is considered the equivalent of "unhappiness." We believe that these symptoms are familiar to almost everybody, so that even when elicited by different examiners in different groups of patients they are roughly comparable.*

anxiety neurosis. In a follow-up study of the latter cases[7] it was found that the symptom of effort trouble was as prevalent at the time of follow-up as it had been at the time of hospitalization. The chronicity of this particular symptom might be related to a constitutional (genogenic) factor. In Table 5 of the paper by Wheeler and others[3] the symptom "tires easily" (effort trouble) is shown as present at the time of follow-up in 47 of the 60 patients. This was the same incidence as at the original examination; in 9 cases the original symptom had disappeared, in 38 it had persisted and in 9 it was newly recorded at follow-up.

Other Disorders with Similar Symptoms

What further can be said about other illnesses in which symptoms of breathlessness, palpitation,

nervousness and fatigue occur? Is an all-inclusive diagnosis satisfactory, or can real differences be shown to exist? Here the evidence comes from the accumulated information regarding psychologic factors that are associated with the symptoms. In the previously mentioned papers on NCA[1-4] there is an implicit disregard of the importance of psychogenic factors. We disagree strongly with this and maintain that of the multiple etiologic factors in the neuroses the psychogenic ones are by far the best understood and the most accessible to study at the present time. There is enough specificity in certain syndromes to warrant their being separated on the basis of their symptoms and psychopathology into such categories as hysteria, morbid grief reactions, reactive depressions, obsessive-compulsive neuroses, hypochondriasis and so forth. Any of these conditions can at times present an array of symptoms that would meet the criteria of NCA,[2] yet with respect to some of their basic features, such as psychodynamics and responsiveness to certain forms of therapy, they are not really similar. It must be re-emphasized that our present systems of classification are not satisfactory and that many psychoneurotic reactions do not present a clear-cut structure and must therefore be designated as "psychoneurosis, mixed type," but this specific inadequacy is hardly a valid objection to naming those syndromes that are reasonably distinct and widely recognized. Four case histories are presented to illustrate how patients may have these certain symptoms in common and yet have different psychopathologic conditions.

Case 3. Mr. B., a 22-year-old single man, had been troubled for 6 years by a compulsion to repeat actions and thoughts. The symptom had become worse after he took a job on graduating from high school, and much of his time was spent in counting everything — the steps he took, the pages he read and so forth. Because of irrational doubts he had to check and recheck even the simplest acts.

The patient also had episodic symptoms that he associated with periods of "emotional tension"; these included palpitation, uneven respirations and sighing. At times he felt "nervous" and irritable and complained of fatigue, headache, anorexia and backache. He was noted to be very neat in his dress and grooming, and he said it made him uncomfortable to need a bath or to have dirty fingernails.

In psychiatric interviews the patient's father loomed as a very important figure. He was described as stubborn, domineering and harsh. The patient's compulsive acts, daydreams and indecisions were interpreted as protective devices — protecting him from the strength of his impulses, which if allowed free rein would have resulted in guilt and opprobrium. It was not possible to elucidate the origin of the intense hostility toward his father, but it appeared that his only means of dealing with it was the neurotic mechanisms. The symptoms of "neurocirculatory asthenia" seemed no more than the somatic manifestations of anxiety.

Comment: This young man had a typical compulsion neurosis that was accompanied by some signs and symptoms of anxiety. The psychodynamic factors of the neurosis could not be ascertained in brief psychotherapy, but there was evidence that a deep and intense hostility toward the father was very important. In general this type of neurosis tends to be chronic and is not often influenced by brief psychotherapy.

Case 4. Miss J., a 31-year-old unmarried woman, was referred to the Psychiatric Service because of a 3-day period of complete amnesia. Interviews soon revealed that this episode was only one in a long series of symptoms and interpersonal maladjustments. She had had an unhappy childhood, of which the most significant feature was her ambivalent feelings toward a strict elderly father. Two and a half years prior to the amnesic period, her younger brother, to whom she was much attached, died of an acute illness. This loss disturbed her greatly, and she dwelt on it at length in the interviews. After he died she felt "emotionally dead." Then, without any awareness of her motives, she had allowed a 50-year-old man whom she hardly knew to have intercourse with her. She said that the experience was very unpleasant, and she could remember only vaguely what had happened.

Later other symptoms appeared: "drawing feelings" in the left chest, difficulty in breathing, dizziness, palpitation, chronic fatigue, indigestion and backache.

As the interviews progressed, she spoke more of her attitude toward sexuality. She stated that except for the inexplicable indiscretion after her brother's death she had not been interested in men. In fact, she regarded sex with fear. When she was 15 a middle-aged neighbor had tried to rape her; after this experience she had felt guilty and "dirty." For a time she had had a mild compulsion in the form of bathing 3 to 4 times a day. She avoided reading love stories and romantic novels because they made her "so tense."

Despite her conscious feelings, she had become involved in a number of sexually exciting episodes, as, for example, with a 60-year-old minister who wanted to leave his wife and take the patient to another city. Such situations, however, never eventuated in intimacies.

Considerable therapeutic work was devoted to attempts at clearing the amnesia, with partial success. It developed that the patient had spent the 3 days in a rooming house in a nearby city, and the evidence suggested that she had been accompanied, at least part of the time, by a man. She never admitted recalling what happened but expressed fears that she might have been seduced. She was much relieved when her menstrual period appeared a week or so later.

During the course of therapy she developed a strong attachment to the psychiatrist, with many sadomasochistic fantasies. Her oedipal conflicts were clearly expressed in the interview material, and her erotic fantasies were noted to contrast with her conscious expressions of fear and disgust in regard to sexuality.

Comment: This case illustrates most of the classic features of hysteria. The mechanism of repression (amnesia for a traumatic event) is clearly seen, as well as the characteristic sexual conflicts. There were also some symptoms of anxiety. The backache appeared to be a conversion symptom, and its relation to the sexual "acting out" after her brother's death was revealed in the interviews.

Case 5. Mrs. R., a 30-year-old widow, had numerous symptoms that had developed after tragic personal losses. Her young daughter had died of peritonitis, and the patient had gone through an exhausting vigil at her deathbed. After this experience she noted the onset of chronic fatigue, which did not respond to rest. She reported that after her daughter's death she tried very hard "not to think about her." For a year she managed to get along fairly well until, in a situation that partly reproduced the mother–daughter relation, her unresolved conflicts with the dead child were reactivated. She began dreaming of her daughter, often seeing her in pain — "she was suffering and no one would help her." At this time anxiety attacks commenced, characterized by dyspnea, palpitation, sweating and a sense of impending death. She also felt faint, dizzy and weak, and her fatigue became worse.

Four months after the onset of the anxiety attacks, her husband, brother and father were all drowned in a fishing accident. From that time until her admission to the ward

she wept a great deal, was very depressed and was so tired that she could barely force herself to do the housework.

During 8 weeks of psychotherapy she discussed her symptoms at length. She was encouraged to talk about her relations with her husband and daughter, and the interview material pointed clearly to the connection between their deaths and the patient's symptoms. Anger directed toward them had not been consciously accepted, and it seemed clear that this hostility (associated as it was with their deaths) produced so much guilt in her that she believed that she too had to die. The patient was of limited intelligence and did not obtain any real insight into her ambivalent feelings. However, the discussions of her bereavement and subsequent illness did seem to help her; the symptoms gradually abated, her depression and fatigue lessened and several of her dreams indicated a wish to dispense with mourning and to put on brightly colored clothes again. She was given encouragement and emotional support in the direction of resuming a fuller, more active life.

The patient was discharged markedly improved, and when seen for a follow-up interview 3 years later she considered herself "almost 100 per cent well." She still felt lonely and tired at times and had not remarried. She said that if the "right man came along" she would like to remarry; she believed that that would relieve the residual feelings of loneliness.

Comment: This case was diagnosed as a "morbid grief reaction" but could also be regarded as a reactive depression. It might be said that psychotherapy was unnecessary here — that time would have healed her psychic wounds. This may be true, yet the patient did seem to be helped in a relatively short time by "working through" her grief reaction.

CASE 6. Mr. S., a 35-year-old married man, had numerous complaints. He said that "gas on the stomach" was pressing up on his heart, and he also had the fear that his stomach had dropped. His symptoms were bizarre; for example, he described his feces as "red, yellow and black, like rotten meat," and he was convinced that light entering his eyes made him nervous, because if he kept his eyes shut he felt better. He feared that his body emitted a bad odor. In addition to the above complaints, he had had other distressing symptoms for several years: difficulty in getting his breath, spells of rapid heartbeats, faintness, weakness and dizziness.

In interviews the patient talked of his many inexplicable somatic sensations and fears and also told of his interests and hobbies. He had spent much time developing a set of astronomical theories and had been absorbed in drawing designs for aircraft engines, which he had submitted on occasion to Government agencies. He displayed to the psychiatrist a large number of surrealistic drawings that were quite weird in their content and symbolism. These latter aspects of the illness were purposely ignored during treatment, the emphasis being placed on the anxiety symptoms. Reassurance and the development of a friendly relation with the therapist seemed to help him a little. At a psychiatric staff conference the question of diagnosis was discussed at length; most of those present believed that he was not schizophrenic. The final diagnosis was hypochondriasis and schizoid personality.

Comment: From the psychologic standpoint, the dynamics of an illness such as this are quite different from an ordinary "anxiety neurosis," and it has been found by experience that the prognosis for "recovery" is usually unfavorable and that brief therapy of any kind is rarely successful.

These cases, of course, are exaggerated examples, chosen purposely to highlight the fallacy of picking out a symptom complex and regarding it as a disease entity. Obviously, few physicians would mistake hypochondriasis or obsessional neurosis for the sort of illness illustrated in Case 1, yet all such patients as these may have the diagnostic triad of NCA.[3]

DISCUSSION

Further discussion is indicated concerning why the syndrome of NCA cannot be delineated precisely and why many of the studies on this subject have not been fruitful. The great complexity of any investigation of human maladjustment is one obvious factor, but other reasons appear as well. Much of the research on NCA patients has been too narrow in its scope. Emphasis has been frequently laid on attempts to find "organic" abnormalities to "explain" the symptoms. Master,[8,9] for example, takes a dogmatic and restricted view of the low exercise tolerance of patients diagnosed as having NCA. He says: "These patients constitutionally are inferior. They are asthenic and usually have a long narrow chest, and it is my opinion that the volume of the heart is small. The vasomotor responses are therefore inadequate. The blood pressure and pulse responses to standard exertion lag. The two-step exercise electrocardiogram may be abnormal. Thus, on exertion they have a functional coronary insufficiency which is probably neurogenic."[9] This opinion, we believe, is true of only a few cases (such as our Case 1) and is not generally accepted by cardiologists who make the NCA syndrome a more inclusive category.

Neurosis from the Dynamic Standpoint

A disease is not an uncomplicated sequence of cause and effect. For example, one cannot be satisfied with the formula "Lobar pneumonia is caused by the pneumococcus." The human organism does not react in part to a stimulus but as a total biologic unit. Overemphasis on the concept of cause and effect leads to oversimplification in medical research; one should, rather, think in terms of *stimuli* and *responses*.[10] A "neurosis" (or "NCA") is a response; as such it is expressed in symptoms, signs and complaints — not only those listed in the definition of NCA[3] but even more varied ones referable to all the physiologic systems. The stimuli that arouse these responses may not be immediately apparent. A stimulus may be marked by repression and amnesia. For example, a patient may have difficulty in breathing on entering a subway, and no matter how often he repeats this experience or how much he reassures himself, the symptom persists. The stimulus is not the exertion of walking into the subway, nor is it the subway *per se*. The patient himself is unaware of what it is. A clinical example illustrates the point: A man who complained of this symptom was admitted for psychotherapy; it was discovered that the significance of the subway for him was related to his acute conflict over homosexual urges. He had experienced a passive homosexual seduction (fellatio) in a subway toilet room. The shortness of breath that came on when he entered the subway represented his anxiety over the homosexual conflict. Insight into this problem removed the

specific symptom, but the serious neurotic disturbance still existed and was manifested in other ways.

When the stimulus can be demonstrated (as in psychotherapeutic interviews) it is observed to have certain characteristics: It usually arouses strong emotion; it has a specific meaning for the patient; and it generally has a symbolic significance that is specific for some forgotten conflict or disturbing fantasy of the patient. Thus it becomes clear that the symptom itself is less meaningful than the stimulus that sets it off. Moreover, a neurosis is much more than a series of complaints recited by the patient. "Neurotic" responses to stimuli do not necessarily have a symptomatic expression; more subtle manifestations can be studied, such as character traits, patterns of social response, variations in bodily posture and so forth. In the absence of a satisfactory *definition* of psychoneurosis, one might discuss further some of the attributes that are important from the psychodynamic viewpoint — more significant than a list of symptoms. A brief presentation of the concept of anxiety is pertinent here. Anxiety is an emotion familiar to all of us as a diffuse uneasiness or apprehensiveness. In psychoanalytic theory it is thought of as an intrapsychic "danger signal" that appears when the personal integrity of the individual is threatened. The somatic manifestations are similar to those of fear and include shakiness, palpitation, shortness of breath, urinary frequency, sweating and so forth. In the face of real danger it is normal to be afraid and to have symptoms as described above. When the danger is internal (such as some primitive drive that is not compatible with one's conscience) anxiety is the reaction to this threat and is a signal for mobilization of stronger psychologic "defenses."

Stated in its simplest form, the psychoanalytic theory of the psychoneuroses holds that not only neurotic symptoms but many character traits and even complex patterns of social adjustment are determined by the patient's need to avoid conscious anxiety. It is not pertinent here to elaborate the evidence for or against this theory; suffice it to say that in treating patients one is impressed by the fact that more or less well defined clinical syndromes are associated with characteristic "ego-defense mechanisms" and that when these neurotic defenses are broken down the patient experiences anxiety.

In patients with obsessive-compulsive rituals, such as compulsive hand washing, the symptom may be understood psychologically as a form of behavior that wards off anxiety. In cases where psychoanalysis has revealed the significance of the symptoms, obsessions and compulsions are usually found to represent prohibitions, atonements or substitute gratifications. The wish or drive that cannot be acknowledged consciously is dealt with or satisfied in a symbolic manner. If the patient is prevented from carrying out his obsessive or compulsive ritual, overt anxiety frequently appears.

The term "hysteria" (probably securely imbedded in medical language despite its inept derivation) is customarily used to designate patients who show childishness, amnesia and "conversion." The latter is understood to be a psychologic mechanism by which the patient "converts" a repressed wish into an overt and incapacitating symptom. The impulses that are forbidden access to consciousness are usually sexual or hateful or both; the symptom then serves as a solution of the conflict and relieves the patient of the necessity of facing it.

It will be seen from the foregoing discussion that so many variables contribute to the development and dynamic characteristics of a neurosis that it is impossible to set up a scheme of partitioning that is at once simple, objective and clinically useful. Although we have stressed the point that symptomatic resemblances can be misleading, it is nevertheless true that some of the generally accepted diagnostic categories (such as hysteria and obsessive-compulsive neurosis) do have more or less typical "symptomatic profiles" that are related to the underlying psychopathologic processes. This is probably because most persons of our culture react somewhat similarly to similar situations. The important thing to each person, however, is the meaning to him of the stimulus — what there is in the given situation that brings out the neurotic response. This is entirely missed unless the patient is understood psychologically in terms of his own unique life conditioning and certain impulses and conflicts of which he is not consciously aware. No amount of listing of symptoms will ever explain what is going on.

Our major disagreement with the catch-all definition employed by Wheeler and others[3] is that it includes under one heading a variety of illnesses. The postulation of a disease entity so protean in its manifestations as to be synonymous with "psychoneurosis," "shell shock," "combat fatigue,"* "vasomotor instability," "irritable heart" and "cardiac neurosis"[1] makes diagnosis very simple but is an impediment to further understanding of psychologic and physiologic mechanisms.

Physiologic Observations

When patients with psychoneuroses or those diagnosed as having NCA have been compared to healthy persons under various experimental conditions, no *qualitative* differences have been demonstrated in the various physiologic, biochemical or hormonal systems. Some *quantitative* differences have been shown, especially in oxygen utilization and lactic-acid production during and after ex-

*The term "combat fatigue" was not used as a definitive diagnosis in the armed forces. It was a label of expediency to be put on field medical tags of soldiers who were to be hospitalized for neuropsychiatric study and treatment.

ercise,[11-15] but these are not unequivocal.* No significant differences in response to submaximal exercise could be demonstrated when psychoneurotic patients were compared with *untrained* healthy controls in a recent study.[15]

The main facts that have emerged from reviewing a mass of research data[19] are that psychoneurotic patients (as contrasted with healthy persons) have a relative instability of various physiologic systems and a tendency to over-react to different stresses. The degree of physiologic instability seems to correlate roughly with the amount of anxiety experienced by the patient,[20] but the significance of this relation is not known. It seems entirely possible in the light of current neurophysiologic theory that in a psychoneurosis or a psychosomatic disease there may be some anatomic disorganization, such as a disturbance in the reverberating circuits of the cerebral neurone chains.[21] If this proves to be true, it would in no way threaten the validity of psychologic observations or the importance of the psychogenic factors in the neuroses.

If response to exercise is selected as the decisive characteristic on which to base a division into two groups, the work of Jones and Scarisbrick[12] is significant. Their study of soldiers diagnosed as having NCA suggests that a quantitative physiologic difference exists between those whose effort intolerance had been a lifelong symptom and those who had been reasonably good athletes until the onset of their illness under the stress of military service. (This finding is consistent with our view of "NCA" and "anxiety neurosis" as opposite ends of a continuum, with the former diagnosis reserved for those patients who have evidence of a constitutional physiologic deficit.)

Shands and his associates[22, 23] have studied a large number of psychoneurotic patients who complained of fatigue states and note that "the feeling of tiredness is specific for certain activities; whereas at times the patient can carry on strenuous activities of one sort, other forms wear him out at once." The ability to perform exercise certainly bears a close relation to motivations and psychic conflicts. (Some of Shands' patients were among the group[18] that showed no significant differences in response to exercise as compared to healthy controls.)

Wolf and Wolff[24] reported the reactions to standard exercise of a healthy person studied daily for ten months. During a period of tension and anxiety associated with emotional conflicts his physiologic reactions to the standard exercise became similar to those of a patient with NCA. His pulse rate, blood pressure and cardiac output were elevated markedly over their customary post-exercise levels. Moreover, he was dyspneic for a longer period after exercise than on other days and his ventilation rate was three times the usual level after the same amount of exercise. The post-exercise responses returned to their ordinary values when the period of anxiety was over. No lactic-acid determinations were made, and it would be interesting to know whether the lactic-acid production, in response to standard exercise, also varies according to the subject's psychologic state.

The somewhat problematic results of these various investigations might be clarified if the experimental groups were selected more carefully. It is possible that the patients whose symptoms are almost purely psychogenic would be the ones to show no significant changes in oxygen consumption and lactic-acid production even if they developed hyperventilation, dyspnea and fatigue. In order to test this idea, however, one would need a more dynamic point of view than is possible with the diagnostic criteria that we have criticized.

NCA, Psychoneurosis and Anxiety Neurosis

The foregoing discussion has been elaborated to furnish a background for the questions posed earlier in this paper. By now it is clear that NCA (as defined by Wheeler and others) covers in blanket fashion many of the psychoneurotic syndromes. We have already expressed our opinion of the undesirability of such a loose definition. We believe that the question whether NCA is identical with anxiety neurosis must be answered by a qualified "no." For the reasons already given, an unequivocal distinction is not now possible and perhaps never will be, even if the definitions of NCA and anxiety neurosis are made more precise.

The Value of a Dynamic Orientation

If we are to be able to evolve more operationally useful diagnostic categories and increase our knowledge of the fundamental biologic disturbances in the neuroses we must study the responses of the patient as a whole in his attempts to maintain an adjustment to his environment. The patient's inborn (genogenic) physiologic "strength" or "weakness" with respect to different stresses is certainly important, and one hopes to learn eventually how to define and measure it; investigations must also continue on chemogenic and histogenic factors. We hope to have illustrated convincingly the importance of psychogenic factors.

The reluctance to search for and recognize psychogenic factors seems to be rationalized by some investigators on the grounds that such data are not "objective" or "scientific." However, a methodology in which there is no place for observations unless they can be measured on a finite scale and treated by statistical analysis denies a place for simple observation of phenomena, the basis of all natural history. A quotation from Mishkin[25] impressed us as unusually apt. In commenting on the futility

*Dr. Mark D. Altschule called to our attention the observation of Hurst[16] that a similar disturbance of lactate metabolism during exercise occurred in schizophrenia, which Hurst associated with the fact that the patients were physically "out of training." Manic-depressive patients also may show a large rise in blood lactate after exercise,[17] although the data on this are inadequate.

of much of the older work in physical anthropology he says that preoccupation with measurements alone "not only produced the illusion that we were in the possession of real knowledge but it poisoned the work of the new generation of anthropologists." He also remarks, apropos of this type of scientific method: "But the great tragedy was the invention of the calipers. Give a man a measuring rod and he will use it to beat his brains out. . . ."

Two cases chosen (like our Cases 1 and 2) to illustrate a certain point can be more significant than a long uniform series. Four cases (like our Cases 3–6) that prove exceptions to a postulated rule can upset a thesis based on fifty or a hundred routine observations.

In the problem of evaluating follow-up results[7] and attempting to learn if, how and why treatment has influenced the course of the illness, the importance of a dynamic formulation is obvious. An arbitrary label (whether it be "psychoneurosis" or "NCA") tells us almost nothing of the factors that are related to prognosis. A carefully developed appraisal of the significant physiologic, psychologic and environmental factors is the first step in evaluating the role played by therapy in any changes that might occur.

It has been stated, for example,[8] that there is no definite evidence that patients with NCA, anxiety neurosis or neurasthenia treated by prolonged psychotherapy or psychoanalysis progress better than patients who have had little more therapy than simple reassurance and the passage of time. We agree that it cannot be "proved statistically" that psychotherapy actually helps patients, but it is doubtful that anyone who has treated patients with intensive psychotherapy would agree that they do just as well with simple reassurance and the passage of time. It is true that psychoneurotic illnesses often improve without planned psychotherapy. Reassurance, emotional support, environmental manipulation and "spontaneous" changes in life stresses (divorce, marriage, change of job, reclassification from combat duty and so forth) may be followed by disappearance of the symptoms. What has sometimes been overlooked is the significance to the patient of these "nonpsychotherapeutic" changes. If one investigates the emotional needs, conflicts and interpersonal relations of the patient with his pulse, blood pressure, electrocardiogram and spirogram, a "spontaneous" improvement often becomes understandable.

Important aspects of the doctor-patient relation[26] have been overlooked by many physicians. Conscious and unconscious attitudes and emotions that the patient transfers to the physician have much significance. "Simple reassurance" *is* psychotherapy; indeed, sometimes it may be very potent psychotherapy. Of prolonged psychotherapy little can be said in relation to "NCA"; the cardiologists have tried it so infrequently that no data exist to indicate whether it is helpful or harmful. In the case of "anxiety neurosis," there is much clinical experience to indicate that psychiatrists have relieved patients by prolonged psychotherapy. Since the disorders overlap so frequently it is probable that many cases called "NCA" could be helped by psychotherapy.

Unless one makes some attempt not only to measure the constitutional or physiologic factors but also to understand the psychodynamics of the illness and of the therapeutic processes as well, it seems unlikely that even the most objective and scientific investigations can prove fruitful.

Summary

The view of neurocirculatory asthenia as a disease entity identical with anxiety neurosis and psychoneurosis has been examined and criticized. Evidence has been presented for the argument that in cases in which the major symptoms center around effort intolerance and breathing difficulties two extreme prototypes exist: those patients whose effort trouble is largely due to an inherited or developmental abnormality and those patients whose symptoms are psychogenic. Between those poles are many mixed cases. Examples have been given also of important nosologic differences in patients whose symptoms might be considered diagnostic of neurocirculatory asthenia. Four common disorders were shown to be characterized at times by the "NCA syndrome."

The difficulty of developing a satisfactory system of classification for the various psychoneurotic illnesses has been discussed in terms of the multiple etiologic factors involved and in the light of the concept of disease as a maladjustment of the total human organism to its environment.

The vagueness of the term "neurocirculatory asthenia" when defined merely by a list of symptoms results in confusion and increases the difficulty of interpreting research data. It is urged that investigators whose interests and orientation are primarily physiologic should be more aware of the psychodynamic differences among patients who resemble one another symptomatically.

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CONTROL OF INOPERABLE ORAL CANCER WITH MASSIVE ROENTGEN THERAPY*

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THE control of inoperable oral cancer is important not only for cure of the localized lesion but also because the subsequent treatment of involved regional nodes must usually await the successful eradication of the primary disease. Radiation therapy is generally considered the only effective approach to those carcinomas of the mouth that cannot be eradicated surgically. Although many of these lesions are controlled by conventional dosages, experience at Pondville Hospital has suggested that there are too many patients in whom the primary disease persisted or recurred after conventional x-ray therapy had been administered.

In 1946 a more radical regimen was instituted in an attempt to achieve better control of the primary carcinomas of the mouth. This program consisted simply of greatly increasing the tumor dose in conjunction with technics designed to minimize the amount of radiation to the normal tissues. The higher tumor dose appears to control the relatively radioresistant carcinomas, assuring a better cure rate in patients whose disease is confined to the mouth. The data also suggest that surgical treatment of metastatic nodes can be instituted without a long post-radiation interval to determine whether the primary disease is controlled. In many patients, operable nodes in the neck become inoperable during the period of observation, thus diminishing the chances of cure in those patients. The same principle applies to those cases in which radium and roentgen therapy are used to treat inoperable neck nodes. Earlier treatment of the metastatic disease, either by surgery or by radiation, will yield a greater number of cures.

During the period of this experimental study all patients were accepted for treatment, regardless of the extent of the primary lesion or of metastases. We concerned ourselves initially with only the status and response of the primary disease and excluded the metastatic nodes in this phase of the treatment. This concerted attack on the primary disease seemed to be the most effective approach to the problem. This policy naturally resulted in the treatment of some patients with advanced disease, in whom the prognosis was inevitably poor. Most of the patients were elderly. All the lesions treated were proved epidermoid carcinomas, and no treatment was modified by histologic grading. No patients were lost to follow-up.

When patients were first seen every effort was made to improve the status of oral hygiene, which was usually poor. The dental department was of invaluable aid in this respect. Many patients had infected carious teeth and chronic infection in the soft tissues. As a general policy we required extraction of all teeth prior to radiation therapy. This recommendation was easily accepted by those elderly patients who had but few remaining teeth, these usually being in poor condition. There was often resistance on the part of patients with a full set of healthy teeth, who were understandably reluctant to part with all their teeth. However, we still insisted on removal of at least all those teeth that were located in the path of the x-ray beam, particularly in the lower jaw. The extraction of all teeth was advised because we believe that it removes a potential cause of radiation necrosis of

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the jaw. The heavily radiated mandible becomes atrophic, and its marginal status renders it susceptible to any trauma or infection, which may in turn precipitate overwhelming radiation necrosis. If the teeth are allowed to remain in the jaw they may become carious or infected. Their treatment or removal represents a traumatic insult to an already atrophic mandible. The second reason for extraction of teeth applies to those cases in which there is local infection that can be eliminated only after removal of infected teeth. The third reason is a technical one, namely, to allow the use of a large intraoral portal. The importance of the large intraoral portal is readily appreciated if one realizes that almost half the tumor dose is delivered through this route, with no external skin surfaces involved. After the intraoral infection had been controlled and the teeth removed, there was usually a waiting period of five to seven days before x-ray therapy was instituted. This interval was usually sufficient to allow healing of the gums. We have generally attempted to hospitalize these patients, because the preparation for x-ray therapy can thus be accomplished more quickly. In addition, hospital nursing care is an important factor during and immediately after x-ray therapy.

Treatment is generally carried out through one intraoral and three external portals, of which the intraoral portal is probably the most important. Every attempt is made to use a portal large enough to include at least the tumor and an adjacent margin. The average diameter was 4 cm. Many mouths accommodated a cone 4.5 to 5.0 cm. in diameter. Cones of a diameter of 3.5 cm. or less were seldom used. The size of the cone is limited only by the gingival margins of the open mouth, and the advantage of teeth extraction becomes apparent during this phase of the treatment. In every case the cone was inserted beyond the gingiva, thus excluding any portions of the lips from the field of therapy. The relatively lower tolerance of the lip structures as compared to that of the oral mucosa makes this mandatory. If the end of the intraoral cone is beveled, it is easier to direct the beam more accurately. We do not consider it necessary to apply the cone at right angles to the tumor base; in many cases we were satisfied to direct the portal in a tangential line. Even though the intraoral cone did not include the entire tumor in some instances, it was thought that this portal was effective in erasing the bulk of the lesion; the external portals were depended on to eradicate any remaining disease. The intraoral treatment was given at the rate of 400 r daily, and a total of 6000 r (in air) was delivered through this portal over a period of fifteen days.

The three external portals, including two lateral portals on either side of the jaw and one submental, were employed simultaneously and were directed over the tumor and its margins. These portals vary from 6 by 8 to 8 by 10 cm. The submental portal, usually round and 5 cm. in diameter, was likewise directed toward the tumor site. The three external portals were employed in every case in which the tumor was in or about the midline. When the tumor was on one side of the mouth, as in buccal mucosa, gingival ridge or tonsillar fossa, the contralateral facial portal was excluded because of the relative inefficiency of 250-kv. radiation. During the initial phase of the treatment, therapy was delivered daily through the intraoral portal and one of the external portals. The latter were rotated, so that a different field was used on successive days. It was considered important to deliver the intraoral therapy rapidly because the major portion of the tumor dose was delivered by this route. In addition, the radiation reaction that appears in the late stage of treatment makes it difficult and painful to employ an intraoral portal. In the presence of trismus or severe infection, the intraoral cone could not be used. It was necessary therefore to start with the external portals, hoping that the regression of the tumor and the infection would reduce trismus and allow the use of the intraoral portal later. Treatment factors are as follows: Intraoral portal — 250 kv.; 15 m.a.; 0.5 mm. Cu plus 1.0 mm. Al. filtration; 40 cm. distance; 400 r daily. External portals — 250 kv.; 15 m.a.; 0.5 mm. Cu plus 1.0 mm. Al. filtration; 50 cm. distance; 200 r at each treatment.

The first phase of the treatment consisted of the employment of the intraoral portal and one external field daily until the completion of the intraoral therapy. After the intraoral treatment had been completed, two external portals were treated daily, these being rotated when three were used. The rotation of the fields was permissible because the tumor received continuous daily treatment while some of the external skin surfaces were given corresponding rest periods. No effort was made to include purposely any metastatic nodes during these treatments. If any metastatic nodes were in the field of treatment, this was accepted only as incidental therapy. The treatment of these neck nodes was considered as an entirely separate venture. We did not administer more than 3000 r to the external fields, in order to preserve the skin and underlying tissues for further treatment of the positive neck nodes.

At the end of two weeks a radiation mucositis was well established, and the tumor had usually shown definite regression. As the external therapy was continued, radiation changes in the mouth progressed, with continued regression of the tumor. By the time the radiation therapy was completed the radiation reaction was at its height (intensive) and the patient was definitely uncomfortable. At this stage the tumor was usually no longer visible. During the latter phase of treatment careful attention was paid to oral hygiene, and chemotherapy

was often employed as a prophylactic measure against any possible infection. The avoidance of infection is important in the prevention of radiation necrosis of the soft tissues or bone. In most of the cases the tumor dose varied between 9000 and 12,000 r. The entire course of treatment generally required about thirty days. At the end of treatment, nursing care became a very important factor, as the patients were generally reluctant to eat proper amounts of food. The aid of a dietitian was enlisted in order to supply soft food of high nutritional value. The patient required encouragement and constant assurance that the reaction would subside. The reaction of the external skin was usually only moderate; the skin recovered rather promptly. The radiation reaction within the mouth was quite intense and lasted longer than the reactions noted after conventional doses of radiation therapy. Radiation reaction in the mouth regressed slowly and only showed complete regression after about three months. The patient's stay in the hospital depended on the recovery from radiation reaction and his ability to return to a normal diet. He was discharged only when he was able to fulfill the requirements of diet and mouth hygiene at home.

It was considered advisable to modify this program when treating the elderly debilitated patient who probably would not tolerate the maximal tumor dosages. The dosage levels were decreased, particularly through the intraoral portal, but the ultimate tumor dose still remained higher than that given under conventional methods. The same modification was employed in treating the postoperative recurrent carcinoma and in those mouths in which the soft tissues had been altered by long-standing chronic infection.

Results

As has been indicated previously, the primary purpose of this study has been to determine whether or not a change in therapeutic approach, namely, the delivery of a large tumor dose, had effected more satisfactory results in the management of intraoral cancer. In order to evaluate the effectiveness of this program, we have compared the results of the radical approach described with those achieved in a comparable group of patients treated prior to 1946 with conventional therapy. The two groups are distinguished only by a difference in the tumor dose delivered. The experimental group comprises a series of cases treated with massive doses of radiation; a tumor dose of 7000 r has been taken as the minimal level for inclusion in this group. Most of these cases have been treated since 1946. The control group was treated from 1944 to 1946. It might be well to emphasize that all cases of intraoral cancer treated primarily by radiation during the period from 1944 through 1949 have been included. A tumor dose of 7000 r has been used as an arbitrary boundary separating the two groups. As will be apparent later, there was a distinct cleavage on this basis. Time alone could not be used as a basis of segregation, as the program of massive therapy was not uniformly adopted at the outset.

It is now generally accepted that the only satisfactory method of expressing the amount of radiation delivered to a tumor is through exact specification of a tumor dose. Unfortunately, tumor doses were not calculated in many of the early cases reviewed in this study; consequently, it was necessary to estimate the tumor dose. Since excellent descriptions of the location and extent of the lesions were available, this was a relatively simple procedure that could be done with reasonable accuracy. The maximum error is believed to be less than 10 per cent, a figure that could have no important effect on the results to be presented.

Table 1 shows the total number of cases of cancer seen at Pondville during the study period; against these are listed the intraoral lesions for that period. It is of some interest to note that the cases of intraoral cancer constitute a significant proportion of the total, namely, 7.2 per cent. Over the period of years studied, there has been no important change in the total number of lesions of this type or in the percentage of total cases of malignant disease, thus suggesting that the groups under consideration are comparable.

Table 1. *Relative Incidence of Intraoral Cancer* (Pondville Hospital, 1944-1949).*

Year	No. of Cases of Intra-Oral Cancer	Total No. of Cases of Cancer
1944	41	505
1945	39	495
1946	37	516
1947	40	589
1948	35	558
1949	36	481
Totals	228 (7.2%)	3144

*This includes buccal cavity, floor of mouth, palate, tongue and tonsil.

Table 2 is a summary of information concerning both control and study groups. With regard to the data, it must be emphasized that we have been concerned only with the primary lesion. Where recurrence is noted, this refers only to the primary disease. The total number of cases seen at Pondville during this study period was 228 (Table 1). Of this number 118 patients, or approximately 50 per cent, have been treated primarily by radiation. The remainder were considered satisfactory candidates for surgical therapy. As a general rule, the cases referred for radiation treatment were those in which there was some specific contraindication to surgical treatment. The most common of these were: inaccessibility of tumor (no pharyngeal lesions were treated surgically); such size as to preclude possibility of excision; and general physical condition

contraindicating operation or anesthesia. The number treated is about evenly divided between those receiving massive and those receiving conventional dosage.

Before discussing these data, it might be well to consider certain points of general interest that considerably influence their interpretation. The most important of these, again, is that only the primary lesions have been considered. Figures for persistence and recurrence refer only to the original intraoral lesion. The presence of metastatic disease, even that causing death, is not indicated in the data. If a patient died of metastatic disease one year after therapy but showed at death no evidence of the original lesion in the mouth, he has been listed under the heading: "Dead 1–3 Years with No Evidence of Persistence or Recurrence." Some of those surviving over three years have had operations for metastatic disease, but their primary condition has been treated and controlled by radiation alone.

TABLE 2. *Conventional versus Massive Roentgen Therapy of Inoperable Intraoral Cancer: Results of 3-Year Study at Pondville Hospital.*

TUMOR DOSE	UNDER 7000 r	OVER 7000 r
No. of patients treated	55	63
Average tumor dose	4100 r	9500 r
Persistent or recurrent disease — 1 year	36	16
Persistent or recurrent disease — 1 to 3 years	2	0
Dead — 1 year, no local recurrence	11	12
Dead — 1 to 3 years, no local recurrence	5	10
Living — 1 to 3 years, no local recurrence	0	12
Living — over 3 years, no local recurrence	1	13
Sequelae (radiation ulcer or osteitis or both)	1	14

It should be realized that in general this was a group of elderly debilitated patients. Some died of intercurrent disease. Many presented themselves with advanced metastatic disease that could not be controlled and led to a rapid downhill course even though the primary disease responded well. This accounts for the rather impressive number of patients who have died with no evidence of recurrence of the primary intraoral lesion.

One of the most interesting points to be brought out in this study, — and one that is fundamental to much of the later discussion, — is the time of appearance of recurrences. Of the total number of cases, including those treated with both types of therapy, who developed recurrence (54), only 2 appeared at the end of one year. On this basis we have concluded that the absence of any local lesion at the end of one year is strong presumptive evidence that the local carcinoma has been controlled. The importance of this point in the management of metastases is obvious.

The remainder of the conclusions are fairly straightforward. It is clear that the delivery of tumor dosages in the low therapeutic range resulted in an immediate recurrence or persistence rate of well over 50 per cent. On the contrary, the massive tumor dose effected excellent control. If the patients who died within one year with no evidence of local disease are considered of indeterminate status, the recurrence rates for the high- and low-dosage groups are 30 and 85 per cent respectively. There can be little doubt that this is a significant difference. Of the entire group of 63 patients who received massive therapy, 25 are still alive with no evidence of the local lesion. Thirteen of these 25 patients have survived more than three years since the primary disease was treated. In contrast, the control group shows only 6 patients in whom the primary lesion can be considered to have been controlled. Only one of these has survived more than three years (Table 2).

No effort has been made to present data on the various subdivisions of the intraoral lesions, namely, hard palate, cheek and alveolar ridge, floor of mouth, tonsil and tongue. No strikingly dissimilar results were noted among the groups. The number of hard-palate lesions seen has been very small. Only one such lesion has been treated with massive-dose therapy. Percentage failures of control of the local lesion after massive therapy have been highest in the lesions of the tonsil and lowest in cancer of the cheek and alveolar ridge.

The figures for the mean tumor dose delivered are of considerable interest. It is obvious that there has been a marked difference in the amount of radiation (Table 2). In a few cases tumor doses approximating 6000 r were achieved under conventional therapy. In contrast, few cases in the massive-therapy group received less than 8000 r. Many received over 10,000 r, an amount that may exceed the required cancerocidal dose.

As one might expect, the delivery of such massive amounts of radiation to the mouth has resulted in a certain number of sequelae. These were expected as part of the calculated risk inherent in an attempt to deliver a curative dose.

The only two complications encountered were radiation ulcer and radiation necrosis. Radiation epithelitis, which all the patients displayed before completion of therapy, was not considered in this group but rather as a therapeutic response. Any mucosal defect that persisted or appeared after completion of therapy was considered a radiation ulcer. Any exposure of bone was classed as radiation necrosis.

In the low-dosage group, as might have been expected, there were essentially no sequelae. One patient developed necrosis of the mandible in a lesion of the alveolar ridge. In contrast, the incidence of these sequelae in the experimental group was approximately 25 per cent, equally divided between ulceration and necrosis. In 3 cases the radiation effects were considered a significant factor

contributing to the patient's death. One patient developed necrosis of the oropharynx, which resulted in bronchopneumonia and death. The remaining 2 patients had hemorrhages from areas of radiation ulceration. A majority of the radiation necroses have required resection of the mandible. It is quite possible that more of the cases in the experimental group will develop sequelae in the future. However, even though the sequelae have been distressing for some of the survivors, all have eventually responded to medical and surgical treatment of the radiation necrosis. The close co-operation of the Surgical Department has been an important factor in this program and has undoubtedly contributed in no small measure to the salvage of these patients. In our opinion, the sequelae of massive radiation therapy do not constitute a significant contraindication of its use, in view of the results achieved.

Summary

A method of administering massive roentgen therapy to inoperable intraoral carcinoma is described. This method of treatment achieved much more satisfactory control of the primary lesion than conventional x-ray therapy. The greater assurance of control of the primary cancer thus achieved allows earlier treatment of metastatic neck nodes.

We wish to thank the Dental and Surgical Departments of the Pondville Hospital for their co-operation in this study. We also wish to express our appreciation to Mrs. Ruth Crocker of the Photographic Department.

SUICIDAL DILANTIN (SODIUM DIPHENYLHYDANTOIN) POISONING*

A Case Report

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THE reported incidence of toxic reactions to dilantin (sodium diphenylhydantoin) has varied from 15 to 93 per cent,[1,2] since its introduction by Merritt and Putnam[3] in 1938. These reactions have involved the central nervous system, the gastrointestinal tract, the skin, the gums, the hematopoietic system and, occasionally, the liver.[4-9] To our knowledge, only 3 deaths attributable to dilantin have been reported.[10-12] The purpose of this communication is to report a fourth case in which death was caused by the drug.

Case Report

A 16-year-old girl was admitted to the Medical Service of Gouverneur Hospital on January 12, 1950, with a history, obtained from the family, of having swallowed an unknown quantity of dilantin 12 hours earlier. The drug was used in a suicidal attempt after severe parental chastisement. The medication belonged to the patient's father, an epileptic. There was no history of previous mental or physical illness. Physical examination on admission showed a well developed, well nourished, semicomatose Negro girl. On physical examination the rectal temperature was 99°F., the blood pressure 116/76, the pulse rate 112 and regular and the respirations 16 and regular. The heart sounds, rate, rhythm and size were normal; no murmurs were heard. The lungs were normal. The abdomen was soft, and no abnormal mass was palpable. There were no eruptions on skin or mucosa. Rectal examination was normal. There was only slight muscular response to painful stimuli. The pupils were miotic and reacted poorly to light. The corneal reflexes were barely present. The fundi were normal. The gag reflex was present and the neck was supple. Superficial abdominal reflexes were absent; deep reflexes of the upper and lower extremities were present and equal, though diminished.

Laboratory examination on admission revealed a urine with a specific gravity of 1.020, no sugar, acetone or albumin and an occasional white blood cell and epithelial cell per high-power field. Examination of the blood showed 5,200,000 red cells, a hemoglobin of 15 gm. and a hematocrit of 47. The white-cell count was 6400, with 72 per cent mature neutrophils and 28 per cent lymphocytes. The erythrocyte sedimentation rate was 11 mm. per hour. The blood sugar was 102 mg., the serum calcium 10 mg. and the urea nitrogen 10 mg. per 100 cc. The cerebrospinal fluid showed an initial pressure of 110 mm. of water, with normal response to the Queckenstedt maneuver. The fluid was crystal clear, colorless and acellular and contained 30 mg. of protein and 80 mg. of sugar per 100 cc. No chemical analysis for dilantin was performed. Chemical analysis of stomach washings revealed no trace of drugs.

Gastric lavage was carried out, followed by the instillation of a hypertonic solution of magnesium sulfate into the stomach. The bladder was catheterized with an indwelling catheter, and oxygen inhalation by nasal catheter was begun, to be continued throughout the course.

Within 15 minutes of admission the coma deepened and all reflexes disappeared. By this time intravenous administration of a 5 per cent solution of dextrose in distilled water had been initiated, and analeptic agents were administered through the tubing at intervals of 30 to 60 minutes. These agents were amphetamine sulfate (benzedrine) 40 mg., caffeine sodium benzoate 0.5–1.0 gm. and nikethamide (coramine) 250-500 mg. Vitamin C and B-complex vitamins were also added to the infusion, and intramuscular injection of penicillin was begun. For the next 18 hours the general condition was unchanged. The findings of deep coma, with complete loss of superficial and deep reflexes, miotic, equal pupils, which reacted sluggishly to light, and diminished though bilaterally equal corneal reflexes persisted. The blood pressure, pulse and heart rate were maintained at admission levels. Fluid intake was continued by slow intravenous infusion, and there was no evidence of renal shutdown although the temperature had risen to 101°F.

After some 18 hours of treatment the coma had lessened somewhat, with a return of slight response to painful stimuli and a diminished return of the deep reflexes. In view of the remaining profound depression, it was decided to continue the administration of amphetamine, caffeine and nikethamide. Nevertheless, deep coma reappeared in the following 8 hours. Twenty-six hours after admission a state of clinical shock supervened, with the skin becoming moist and clammy and the blood pressure falling to 86/40. The heart rate increased to 140 beats per minute, with regular rhythm. Five hundred cc. of plasma was administered.

Six hours later an irregular cardiac rhythm was noted, the rate varying between 180 and 220 per minute. An electro-

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cardiogram made at this time showed auricular fibrillation with a rapid ventricular rate, complicated by paroxysms of unifocal and bifocal (bidirectional) ventricular tachycardia, as well as ventricular extrasystoles, and inconstant intraventricular conduction defects (Fig. 1). The over-all ventricular rate averaged 210 beats per minute. At this time the stimulants were discontinued. After about 2 hours of irregularity a regular tachycardia (rate, 140) appeared but was not recorded electrocardiographically. Because of the profound coma, the stimulant drugs were again given as outlined, at 30- to 60-minute intervals.

There was no further change until 38 hours after admission, when the temperature rose to 106.5°F. Urine formation ceased. The pupils then became widely dilated, and 41 hours after admission the patient died.

Autopsy was performed by the Medical Examiner of the City of New York. Pertinent findings were as follows: The brain weighed 1400 gm. and was diffusely congested. There was some pulmonary congestion and severe renal congestion, with punctate hemorrhagic areas in the pyramids. There were a few scattered areas of fatty degeneration in the liver. The other gross findings were normal. Chemical analysis of the stomach, stomach contents, liver and kidneys was negative, but the brain was found to contain 6 mg. of dilantin per 100 gm. of tissue.

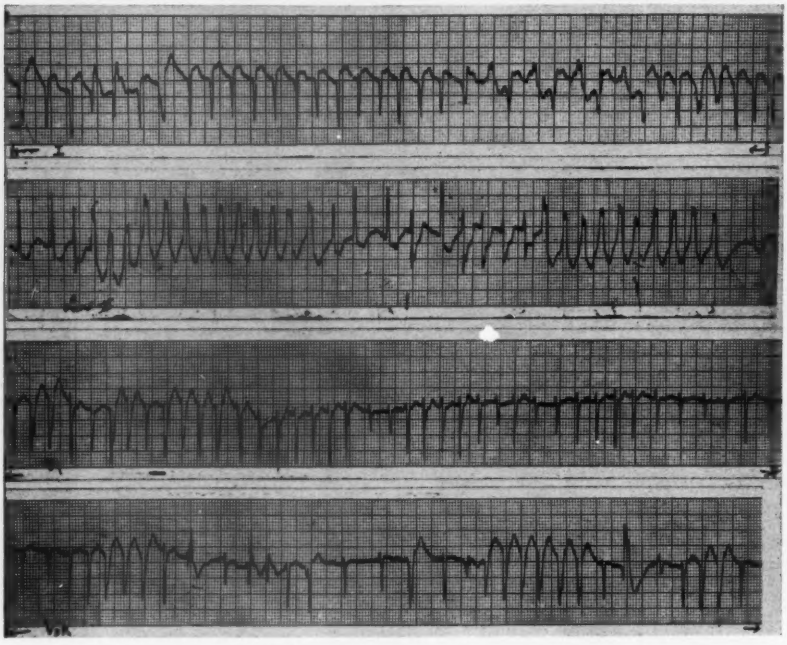

FIGURE 1.

DISCUSSION

The three previously reported cases of dilantin poisoning[10-12] had one feature in common — involvement of the skin, although the character of the eruptions differed. Hemorrhagic lesions were also present in various organs of the body. Our case exhibited no involvement of skin or mucous membranes.

In our case, ingestion of an unknown quantity of dilantin some twelve hours before hospitalization, followed by treatment, led to a fatal termination, with chemical findings of 6 mg. per 100 cc. of the drug in the brain tissue. The similarity of dilantin, nirvanol and phenobarbital[13] led to the treatment of this patient with stimulant drugs in order to affect the depressed vital cerebral functions. Because of the persistence of deep coma, massive doses of amphetamine sulfate, nikethamide and caffeine sodium benzoate were given intravenously over a period of forty hours. The total dose amounted to 2.88 gm. of amphetamine, 144 gm. of nikethamide and 72 gm. of caffeine sodium benzoate. Clinically, there was little or no response. Additional measures of gastric lavage, oxygen inhalation and fluid-balance maintenance were also of no avail in this case, since such a large quantity of dilantin was fixed in the brain tissue.

It is noteworthy that the complex cardiac arrhythmias, including bidirectional ventricular tachy-

cardia, occurred only after large doses of the analeptic drugs had been given. It is known that amphetamine, caffeine and nikethamide are capable of increasing myocardial irritability,[14, 15] particularly in large doses. Dilantin itself has no such toxic cardiac effects but rather a uniformly depressant action that results in impairment of conduction throughout the heart.[16] Such depressant effects may possibly render the heart more prone to development of fibrillation.[17] The state of coma, with its concomitant anoxia, may possibly have added to this hazard. One of us has observed a patient with deep carbon-monoxide coma during which bidirectional ventricular tachycardia was present. It therefore seems probable that the arrhythmia was precipitated by the large doses of amphetamine, caffeine and nikethamide in a heart rendered susceptible by an excessive amount of dilantin associated with coma.

The gross finding of a fatty liver, coupled with prior reports,[18, 19] suggests that dilantin may be toxic to the liver. In this regard it has been shown[20] that intravenous dilantin is at first concentrated in the liver. Unfortunately, microscopical examination of the organ was not made in this case.

This report shows that dilantin, when taken in large doses, may be fixed in the brain in fatal concentration. It thus confirms previous experiments on animals.[20]

Unfortunately, the amount of dilantin taken by this patient is unknown. Cases reported by Robinson[21] and Airing and Rosenbaum,[22] in which epileptics ingested dilantin in amounts as large as 4.5, 4, 6 and 7 gm. with prompt treatment and recovery, lead to the hope that most cases will respond in a more successful manner.

Summary

A case of fatal dilantin poisoning is reported. The patient swallowed an unknown amount of dilantin with suicidal intent. Treatment, including large doses of analeptic drugs, was begun twelve hours later; and death occurred forty-one hours after hospital admission. Dilantin was present in the brain tissue in a concentration of 6 mg. per 100 cc.

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ROENTGEN THERAPY IN ACNE*

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X-RAY therapy has been employed in the treatment of acne vulgaris since Gautier[1] reported its efficacy in 1897. Pusey[2] was the first to utilize this mode of therapy in the United States. Technics were rapidly established, and it was soon evident that an efficient tool had been discovered.

Although the majority of adolescent boys and about half of the girls develop some degree of acne, the condition spontaneously clears in a year or two in most young patients. Proper medical and dermatologic management relieves many others. There remains a small group whose condition is singularly recalcitrant, and who may develop pronounced psychologic disturbances as a result. Disfigurement is increased by the acne scars in long-standing cases and may create difficulty when the patient seeks employment. Roentgen treatment will arrest acne in a high percentage of these patients. It will not erase existing scars. A further indication for x-ray therapy appears in the small number of persons in whom acne appears between the ages of twenty and thirty; such cases are nearly always more difficult to control by routine measures.

Unfortunate sequelae of improperly administered radiation for cutaneous and other disorders, as well as of injudicious roentgenography or fluoroscopy, have given rise in both professional and lay minds to fear of x-ray treatment. It is imperative that any form of radiation therapy be given by qualified persons of proper training and adequate experience. It should first be ascertained whether or not *any* form of irradiation has been employed on the affected areas for the same or other disorders. Occasionally patients mistakenly or purposely conceal a history of previous x-ray therapy, to their ultimate disadvantage.

In addition to the utilization of established reputable technics, certain limitations of the radiation therapy must be taken into consideration and any contraindications observed. It is obvious that the development of an acute radiodermatitis as a result of the treatment of any benign cutaneous disorder is to be avoided.

To our knowledge, no study has been made to determine whether or not the accepted x-ray treatment of acne can produce chronic radiodermatitis. This paper deals with observations on a group of patients who had received roentgen therapy for acne, from five to twenty years earlier.

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Method of Study

In the period between 1926 and 1938, 108 patients received 500 r or more for the treatment of acne at the Massachusetts General Hospital. Only 37 of these patients could be located for re-examination five or more years later. This group was augmented by 21 office patients treated with the same technic five or more years earlier. When these 58 patients returned for observation a careful appraisal was made to determine the presence of atrophy, telangiectasia, pigmentary aberrations or other evidence of late roentgen-ray injury. The degree of efficacy of x-ray therapy was noted, and each patient was asked his opinion of the value of the treatment in curing or controlling his acne.

All 58 patients had received essentially the same therapy; the technic employed was similar to that of MacKee[3] and Andrews.[4] Voltage varied from 75 kv. to 100 kv. The face was treated with 2 exposures; each side received 60 to 75 r. Some patients were given an additional central face dose of 15 r. Unfiltered radiation was generally used, but in a few cases light filtration (0.5 mm. of aluminum) was employed. Weekly treatments were administered, and therapy was stopped when complete clearing had occurred. Adverse reactions, such as erythema or excessive dryness, were avoided. During the period of roentgen therapy supplementary measures included general hygiene, proper cleansing measures and in most instances a low-fat diet. Local agents were restricted to mild astringents, usually borated alcohol.

Results

The data obtained from these 58 examinations and from a perusal of the charts were catalogued under the following headings: maximal number of roentgens administered to any area; age of patient and duration of acne at time of x-ray treatment; type and severity of acne; elapsed time after x-ray therapy; residual acne at time of study; acne scars at time of survey; and signs of chronic radiodermatitis.

The results of these observations were studied and the pertinent material tabulated. *None of the patients showed any atrophy, pigmentation, depigmentation or keratoses.* The cases were grouped by therapy totals, as shown in Table 1, to facilitate assay of effectiveness of treatment.

The average age of these patients at the time of x-ray treatment was 21.4 years. The youngest was fifteen and the oldest thirty-eight years of age. The average duration of the acne process had been 5.6 years. The type of acne was classified as papulopustular in 36 cases; 14 were of the deeply indurated

or nodular variety; and the remaining 8 patients had cystic acne. The degree of activity was classed as moderate in 30 cases and severe in the remaining 28.

The average elapsed time after radiation therapy was 11.3 years. The cases were divided into four-year groups, as shown in Table 2. These varying periods of follow-up appeared to have no relation to the outcome, as the indifferent and poor results had all been apparent before the minimum of five years had elapsed.

Thirty-five patients had excellent results, with no residual acne. An occasional lesion had been noted for varying periods of years in 19 cases. The remaining 4 had unsatisfactory results, but only 1 of these showed no improvement.

Some scarring had been evident in all cases prior to x-ray treatment. Twelve patients believed that treatment had improved their scars (which were insignificant). Another 21 had mild scarring. Fourteen showed more conspicuous disfigurement.

TABLE 1. *Grouping of Cases According to Amount of Roentgen Therapy Received.*

TOTAL NO. OF ROENTGENS	NO. OF CASES
500–800	30
800–1000	20
1000–1200	7
Over 1200 (1450r)	1

The other 11 patients showed severe destructive changes.

Various estimates of the value of the roentgen therapy were advanced by the patients. Such statements are difficult to appraise. When the results of x-ray therapy were analyzed according to the amount of radiation administered, it was found that all the poor responses had occurred among those patients who had received less than 800 r. Despite this there was a good outcome in 56.6 per cent of that group. The acne had cleared in 60 per cent of those who had received 800 to 1000 r. Seventy-five per cent of the patients who had been given over 1000 r were cured. Regularity of treatment appeared to favor a good response and fewer recurrences.

RADIATION SEQUELAE

None of the 58 patients exhibited the classic stigmas of late radiation injury, that is, atrophy, pigmentary changes and telangiectasia. No case showed any two of these signs. Telangiectasia was observed in 9 patients, but this alone is not adequate to signify late x-ray effect. These patients were from thirty to forty-one years of age (average 36.6 years) when examined. Five had received less than 800 r; only one had received 1200 r. Distention of vessels was minimal and was restricted to the malar prominences in 4 cases. The dilatation was such as might be expected from protracted exposure to the sun. One patient showed a peculiar spray of vessels that was sharply limited to the distal third of the nose; an old fracture was suspected but denied. One patient displayed minute dilated vessels over the entire face in such fashion as to suggest hereditary telangiectasia or severe frostbite; neither diagnosis could be established. The other 3 patients clearly had rosacea. They were older patients (thirty-five, forty and forty-one years of age) who had been treated sixteen to twenty years previously and had received 510 to 710 r; one had rhinophyma.

TABLE 2. *Distribution of Cases by Number of Years Following X-Ray Therapy.*

NO. OF YEARS	NO. OF CASES
5–8	18
9–12	19
13–16	15
17–20	6

In all these 9 patients the telangiectasia was relatively inconspicuous and probably could be attributed to causes other than roentgen therapy. They constituted 15.5 per cent of the 58 cases. It seems likely that any group of persons between thirty and forty years of age would show a similar incidence of telangiectasia without previous roentgen radiation.

Those few patients who had had center-face exposures showed essentially the same results in all respects as the entire group.

No keratoses were noted. This was rather surprising, as some of the patients were well over forty years of age.

One case deserves special mention. The patient had been given 710 r to each side of the face and 150 r to the center, at the age of twenty years. The acne relapsed a few years later, and 10 more x-ray treatments were given elsewhere; the amount could not be ascertained. When examined at forty years of age the patient showed mild rosacea, with an oily skin and numerous sebaceous adenomas. He stated that a carcinoma had been removed from one nasolabial fold two years earlier. It would be difficult to associate this condition with radiation treatments. No telangiectasia was present.

No history of further radiotherapy to any other patient was elicited. If any had been given, it would actually have added to the safety of the treatment, as reflected in the data.

SUMMARY AND CONCLUSIONS

Fifty-eight patients with acne vulgaris were reexamined after roentgen therapy. The period of elapsed time after treatment varied from five to

twenty years. The maximum total number of roentgens administered to a single area ranged from 500 to 1450. Telangiectatic vessels were found in 9 patients; all were probably due to causes other than x-ray treatment. No other late sequelae of roentgen therapy were observed.

Properly administered roentgen treatment of acne, given with accepted technic, may be expected to result in the cure of 60 to 75 per cent of stubborn cases.

No late radiation sequelae need be anticipated, because of the limited fractional and total roentgens administered.

The results observed suggest that those patients who received 1000 to 1200 r in an uninterrupted series of treatments had the best results and the fewest recurrences.

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MEDICAL PROGRESS

CEREBRAL PALSY

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CEREBRAL palsy, formerly known as spastic paralysis, is a term that has been popularized recently through the concerted efforts of various organizations interested in providing medical and social service to patients and in stimulating research concerning this disorder. These patients represent the second largest group of crippled children in the country, cerebral palsy being next to poliomyelitis in incidence.[1] It is currently emphasized that cerebral palsy is no longer to be considered a hopeless condition, but rather that some measure of rehabilitation can be achieved by a majority of patients if the proper facilities are provided. During the past five years diagnostic and treatment centers have been established throughout the country that provide not only medical treatment but educational, social and family guidance as well. The staffs, which include specialists in various fields working as teams, have demonstrated that progress can be made with these patients.

Definition and Classifications

Cerebral palsy is generally defined as a condition characterized by paralysis, weakness, inco-ordination, or any other aberration of motor function due to malfunction of the motor centers of the brain.[2] The limitations of the definition have been recognized in practice, and the suggestion has been made that cerebral palsy be defined as an aggregate of handicaps (emotional, neuromuscular, special sensory and peripheral sensory) caused by damaged or absent brain structures.[3] Other investigators believe that cerebral palsy should be included as part of a broader "brain-damage syndrome," as the patient frequently has not only neuromotor dysfunction but other handicaps such as mental retardation, convulsions and behavior disorders of organic origin.[4, 5]

Six main types of cerebral palsy have been described. These are: spasticity (estimated as 66 per cent of the total), athetosis (19 per cent), ataxia (8 per cent), rigidity (4 per cent), tremor (2 per cent) and mixed (1 per cent).[6] The clinical manifestations have been well described.[6-8] Since there is some disagreement concerning whether or not various types of disabilities can be found in the same person, Putnam[9] suggests a classification based on electromyographic findings. By this method the following physiologic states can be recognized, either alone or in combination: spasticity, athetosis and dystonia, alternating tremor and Parkinsonian rigidity, ataxia and transverse lesions of the spinal cord. Benda[10] has proposed a simplified classification on a neuropathologic basis: spastic-rigidity, pyramidal type, and mixed pyramidal-extrapyramidal types.

Recent advances in neuroanatomy and physiology suggest that there may be real differences between spastic and athetoid patients. Classifications may need to be altered on the basis of evidence recently brought to light in these fields.

Etiology

The precipitating factors in cerebral palsy may be grouped in three categories: prenatal, paranatal and postnatal.

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Prenatal

Prenatal factors are considered to be genetic (hereditary) or environmental (exogenous). Genetic factors usually cause defects of the central nervous system such as rudimentary pyramidal tracts, defects of the cerebellum and so forth, and result in such clinical conditions as spastic paraplegia, atonic diplegia, familial athetosis and congenital ataxia.[2, 11-14] Murphy,[15] studying 895 cases of congenital malformations, reported anomalies of the central nervous system in 60 per cent of cases.

Among the prenatal environmental causes, much attention has been given recently to maternal infections by neurotropic viruses, many of which involve the fetal brain. Rubella occurring between the second and fourth months of pregnancy,[16] chicken pox, herpes zoster and influenza[17] have been established as causes of fetal congenital defects and encephalitis.[18] However, recent statistical data reported by Lamy and others[18a] do not substantiate the etiologic role of rubella and other viral diseases in cerebral palsy. Rather, this study suggests that if a neurologic syndrome appears in a case of viral disease during pregnancy it is more or less fortuitous.

Toxoplasmosis, due to protozoan toxoplasma, may result in hydrocephalus, microcephalus, convulsions and motor impairment in the newborn.[19, 20] Endocrine imbalance in diabetic mothers results in toxemia, premature labor and uterine inertia. There are frequent pathologic changes such as jaundice, atelectasis, congenital anomalies and hypoglycemia in the offspring who survive the high fetal mortality rate of 8 per cent.[21, 22] Toxemia of pregnancy, though not a directly demonstrated cause of brain damage, predisposes to asphyxia and prematurity.[23, 24]

Nutritional and vitamin deficiencies, although not clinically proved to cause brain damage, have been found to be causative factors in prematurity and congenital malformations in experimental studies in rats.[25, 26] Recent statistical and neuropathological studies have connected these deficiencies with prematurity and brain damage in human infants,[27, 28] but the results have not been completely accepted.[29]

Rh incompatibilities between mother and child are another important etiologic factor. It has been estimated that 8 to 38 per cent of the children surviving erythroblastosis fetalis have cerebral defects resulting from kernicterus.[30-33] Prematurity, cerebral hemorrhage and maternal diabetes have also been shown to be associated with kernicterus.[34]

Paranatal

Birth injuries resulting from anoxia or trauma play a very significant role in etiology.[35, 36] Anoxia is the most important cause of birth injury.[37, 38] Outstanding causes of anoxia in the paranatal period are: excessive anesthesia during labor, especially nitrous oxide anesthesia (reduction of oxygen tension of maternal blood) or anesthetics that lower systolic blood pressure[39]; oversedation by barbiturates, morphine, scopolamine[40-42]; abnormal deliveries; breech presentations, versions, high-forceps and midforceps deliveries and cesarean sections[43]; induced labor by oxytocics such as posterior-pituitary extracts, which may produce collapse of uterine circulation[44]; cord abnormalities; prolapse[42]; and abnormal twisting.[45] Other causes of anoxia may be interference of oxygenation of fetal blood in the placenta due to a number of factors.[36] Aspiration of amniotic fluid in utero may result in a series of progressive changes, such as atelectasis and pulmonary obstruction, that lead to anoxia.[46, 47]

Since 1862, when Little reported his first cases of spastic diplegia, birth trauma has been considered the principal etiologic agent.[48] Modern authors, however, assign less relative importance to birth injury than formerly.[49] Cephalopelvic disproportions, prolonged and difficult or precipitous labor and injurious complications from instrumentation are considered major causes of cerebral damage. Eastman[39] has shown that the mortality in high-forceps operations is 65 per cent and that of midforceps deliveries 30 per cent. Cerebral disorders were found in 5.9 per cent of infants born by spontaneous deliveries as compared to 23 per cent in infants born by forceps deliveries.[50] Birth injuries may result from vascular trauma of the brain such as subdural or extradural hemorrhage.[51, 52] Permanent cerebral damage from these causes is not now considered as great as was previously believed.[36] Cerebral hemorrhage may also result from increased fragility of the blood vessels, often due to prematurity and hypoprothrombinemia of the newborn.[53] Linear skull fractures may also result from instrumental deliveries and are associated with anoxia and hemorrhage.[51]

Attention has recently been directed to the danger associated with the quickly progressing "normal" delivery. Transient and seemingly insignificant signs of brain damage in the neonate may later attain clinical importance.[54, 55] However, it is rather doubtful that these signs are significant.[56]

Prematurity

Prematurity is the most prominent factor in fetal anoxia. Not only are premature infants more vulnerable than full-term infants to birth trauma and anoxia, but prematurity is more likely to be precipitated by maternal infectious diseases and nutritional and metabolic deficiencies. Moreover, respiratory reflexes in the premature neonate are too undeveloped to respond to ordinary stimuli. There are varied causes of prematurity. Maternal diabetes, toxemia of pregnancy, nutritional deficiency, Rh factor and infectious and chronic maternal diseases are outstanding.[57]

Postnatal Causes

The most important postnatal causes of cerebral palsy are the encephalitic sequelae of infectious diseases such as measles, pertussis and influenza.[58] Postvaccinal encephalopathy following diphtheria,[59] typhoid[60] or pertussis[61] inoculations may result in cerebral damage. Vascular malformations, fractures of the skull with cortical damage and brain tumors may lead to neuromotor impairment.[2] Patients cured of tuberculous meningitis frequently have neurologic and sensory impairment as well as psychiatric disorders.[62]

Cerebral hemorrhage in adults results in neuromotor dysfunction comparable to cerebral palsy in children. Therefore, some present-day workers favor inclusion of this geriatric problem in the category of cerebral palsy.[2]

Physiopathology

The two important physiopathologic factors mainly responsible for brain injury are anoxia and cerebral hemorrhage.

Anoxia

The brain is highly sensitive to lack of oxygen. Inadequate oxygen supply may be considered in a broad sense an immediate cause of death in all fetuses. This may be secondary to traumatic hemorrhage, intrauterine pneumonia, encephalitis or other factors.[2] Fortunately, the fetus is more resistant to oxygen deficiency than the adult, and its survival time is greater.[36]

The important causes of anoxia may be: qualitative changes in the fetal blood in the placenta, low oxygen content due to maternal anemia, cardiac decomposition and so forth; interference with oxygenation of fetal blood due to placenta previa or premature detachment of the placenta; inability of the blood to pass from placenta to fetus due to prolapse or abnormalities of the cord.[63] It is important to know whether one is dealing with anoxic anoxia, in which the prime defect is insufficient available oxygen, or with anemic anoxia, in which oxygen administration is of no value.[64] The principal causes of intrauterine anoxia are thought to be diseases of the placenta or abnormal villi or stroma.[46] About 50 per cent of the mothers of infants with fetal anoxia had complications of pregnancy. In premature infants and infants with brain damage, the low activity of carbonic anhydrase in the blood lowers the speed at which the blood can give off carbon dioxide in the lungs and retards the process of oxygen intake.[65]

Experimental studies in animals have established that fetal anoxia causes neurologic damage before[66] and after birth.[67, 68] However, the relation of duration of asphyxiation to degree of brain damage was less than expected.[68] The structural changes in the brain were multiple petechial hemorrhages, chromatolysis and destruction of neurons. The lesions were predominant in certain areas: the cortex, the tegmentum of the brain stem and the lateral group of the thalamic nuclei. In two thirds of the cases, generalized or regional atrophy appeared eight weeks after asphyxiation. All experimental animals manifested symptoms of a neurologic nature (decerebrate rigidity, hyperkinesia, tremor, spasticities, paralysis and convulsive seizures). Experimental studies in mice showed demyelination in the corpus callosum, the centrum semiovale and the frontal lobe.[67]

Cerebral Hemorrhage

Hemorrhage due to blood-vessel damage is the second most important cause of brain lesions. Various factors may increase the permeability and fragility of the vascular endothelium. The most important one is anoxia, which plays a dual role in causing both primary encephalomalacia and secondary vascular hemorrhage.[2] Direct or indirect trauma to the brain may be precipitated by hypoprothrombinemia, bleeding diathesis, endocrine imbalance and so forth.[12]

The sites of predilection of brain hemorrhage in the newborn are in the vicinity of the large veins and sinuses of the skull, particularly the longitudinal sinus and the vein of Galen. Traumatic hemorrhage generally follows a rupture of these or a laceration of the tentorium with extension of the tear into the sinuses.[36] Autopsies in cases of fetal death have shown that hemorrhages are usually found in the subtentorial space but may be located over the hemispheres. These hemorrhages are primarily subdural or extradural when traumatic factors are involved. However, subarachnoid and intraventricular hemorrhages may exist; these are more often due to anoxic causes or to toxemia.[51] Intracerebral hemorrhages are less common. However, it has recently been shown that bleeding occurs more often in small veins than in large trunks and that blood enters the ventricles and meninges secondarily.[53] The remote effects of the lesions that are not immediately fatal are difficult to estimate, but many brain cells are without doubt permanently damaged.[36]

Neuropathology

A large variety of pathologic lesions are found in cases of cerebral palsy.[69] Josephy[70] emphasizes that there is frequently no correlation between the pathological findings and the clinical syndrome. He has evolved a clinicopathological classification in which the pathological findings may be malformations (defects of corpus callosum, heterotopia, agyria, pachygyria, micropolygyria) or residues of destructive processes (scars, ulegyria, lobar sclerosis, porencephaly, cerebral hemiatrophy, microencephaly). On the other hand, cerebral palsy may be a consequence of well determined morbid entities having a specific etiology, symptom complex and

pathological anatomy, such as toxoplasmosis, Sturge–Weber's disease and so forth.

Lately, Malamud[71] has described status marmoratus not as a disease entity but rather as a sequela of an acquired cerebral lesion, birth injury or encephalitis, that results in a thrombosis of the retinal veins. Quadriplegia, athetoid movements and epilepsy were outstanding clinical features. Carpenter,[72] reporting on athetosis, finds a history of birth injury in almost 50 per cent of the cases studied. The athetosis was frequently a consequence of bilateral status marmoratus of the striatum. However, it must be emphasized that in many cases examination of the brain fails to reveal an anatomic basis for the clinical symptoms.

Neurophysiology

Recent investigations are altering long-standing concepts of the neurophysiologic aspects of cerebral palsy. The theory that spasticity is of pyramidal-tract origin no longer seems entirely tenable. Magoun and Rhines[73] have demonstrated that spasticity results from an exaggeration of spinal stretch reflexes and is influenced by alterations of extrapyramidal cortical areas or pathways connected with Areas 4 and 6. The anterior lobe of the cerebellum is also capable of suppressing the activity of spinal motor neurons.[74]

Another fundamental discovery is that stretch reflexly elicits muscular contraction, which accounts for the substratum of muscular tension that underlies posture. This stretch reflex can be elicited clinically in the child with true spasticity.

In the human infant the midbrain and basal ganglia seem more vulnerable to anoxia than the pyramidal tracts. Athetosis results from lesions in the basal ganglia: putamen, caudate nucleus and tegmental nucleus. The braking mechanism for the steady stream of impulses from the motor cortex fails, and involuntary movements occur. Similar lesions may give rise to tremor. In a recent study Carpenter[72] reconsiders the relation between athetosis and basal ganglia. He differentiates hemiathetosis resulting from necrotizing cerebrovascular lesions of the internal capsule and the striatus and the double athetosis that is mostly due to congenital lesions of the striatum.

Clinical Diagnosis

Many articles have been published that review the diagnostic aspects of cerebral palsy.[2, 4, 35, 76-78] A thorough case history of maternal health, pregnancy, patient's birth, neonatal course and developmental progress as well as a physical and neurologic examination frequently make the diagnosis. Etiologic factors may be single or multiple in any given case.[4, 6, 35, 77, 79] Psychologic tests and laboratory studies pertaining to the central nervous system are helpful in confirmation.

Neonatal

Infants with brain damage may be hypertonic, drowsy or apparently normal at birth, depending on whether the cause is hemorrhage, anoxia or a developmental defect. Intracranial hemorrhage should always be suspected in a newborn who is cyanotic or tense or has twitching or convulsions.[6] Clifford[46] points out that brain damage may be suspected at birth on the basis of the golden color of the amniotic fluid and vernix caseosa and the yellow staining of the infant's skin and nails. Fetal anoxia, possibly resulting from placental disease occurring days or even weeks before birth, produces this syndrome. Levinson[80] has divided neonates with brain injury into irritative and somnolent types and has listed diagnostic criteria for each.

The most common signs of brain damage noted during the early weeks of life have been reported as a poor sucking reflex, poor rooting reflex, lethargy, cyanosis, vomiting, convulsions and variations in body temperature.[35] Other indications of brain damage may be the inability of the child to resist a slow pull upward from the supine to the sitting position,[81] or particular hypertonic postural attitudes.[82]

The newborn with kernicterus, regardless of its cause, appears normal at birth but soon becomes jaundiced and drowsy and has cardiorespiratory difficulties. If death does not occur, indications of extrapyramidal-tract damage become apparent.[83-85] A common resultant clinical syndrome is spastic asymmetric quadriplegia with choreoathetosis. A less common type is the hypotonic-ataxic syndrome.[86, 87] An early sign of brain damage frequently associated with kernicterus may be the so-called peculiar "setting-sun" appearance of the eyeballs,[88] so called because of the prominence of the supraorbital conjunctiva.

Infancy

Physical signs are unreliable bases for diagnosis, since the voluntary motor centers of the newborn are too immature to influence muscle tone.[6] Similarly, reflexes that are abnormal in adults may be normal in infants. Nevertheless, Watkins[78] has described the early physical signs of the common types of cerebral palsy during infancy; in spastic patients there may be stiffness of the limbs or lack of activity of the affected parts. The athetoid infant lies with legs extended and arms and thumbs adducted; increasing numbers of purposeless motions of the extremities are noted. The ataxic infant appears to wish to be left alone, and development is severely retarded. Even in infancy emotional factors may interfere with motivation.[7, 89]

Developmental Diagnosis

Developmental criteria are for the most part exceedingly reliable indicators of brain damage dur-

ing infancy. The principles and methods of the developmental examination have been outlined in detail.[90] Early abnormal neuromotor signs particularly referable to cerebral palsy are failure to achieve head control by three months of age, persistence of clenched fists after four months of age and presence of the tonic-neck reflex after six months of age. Later, minimal cerebral injury may be manifested only as exaggerated startle reflexes, overactivity, minor retardation and speech difficulty. Strabismus is also a common indicator of minimal cerebral injury and is frequently combined with oculomotor inco-ordination. These early signs are frequently overlooked, since they often cannot be detected by neurologic examination.[91] Developmental charts that demonstrate the delays in developmental maturation in children with cerebral palsy as compared to normal youngsters are available for office use.[77, 92]

Childhood

The typical findings in the various types of cerebral palsy usually become fully manifest by childhood. Many children with minor neurologic signs may have mild degrees of cerebral palsy. Strauss[8] has presented a screening plan for this type of case.

Supplemental Diagnostic Aids

Certain diagnostic procedures are helpful in differentiating the various causes of brain damage.

Subdural Aspirations

In the early months of life, although lumbar puncture may be of limited diagnostic value, subdural aspirations are frequently helpful in revealing one cause of abnormal neurologic signs or symptoms. The early removal of a subdural effusion may prevent permanent neurologic sequelae. This procedure is helpful in differentiating idiopathic hydrocephalus, intracranial hemorrhage, complicating meningeal infections, febrile convulsions and subdural effusions.[80, 93-95] As subdural hematomas may be associated with multiple long-bone fractures, x-ray studies of long bones in infants may be helpful.[96, 97]

Electroencephalography

The electroencephalogram has diagnostic and prognostic value in cerebral palsy. Hughes and his co-workers[98] reported electroencephalographic abnormalities in a group of newborn infants who had suffered various types of damage in the birth process. In some instances cortical electric abnormalities were present before clinical signs and symptoms had been observed.

Perlstein and Gibbs[99] reported that 27 per cent of children with cerebral palsy who have no history of seizures show seizure discharges in their electroencephalograms. They found that spastics as a group had the greatest amount of electroencephalographic abnormality, whereas athetoids showed relatively normal findings. There was a striking preponderance of "spikes" in patients with cerebral palsy as compared with a group of unselected epileptics. These were usually focal. Petit mal and psychomotor seizures were rare on the electroencephalographic records as well as clinically.

Aird and Cohen[100] showed results qualitatively analogous to but quantitatively less striking than Perlstein's study. In a preliminary report of the relation between electroencephalograms and eye disorders it was found that electroencephalographic foci in the occipital region occurred almost twice as frequently in the presence of abnormal eye findings in children with organic brain disease causing cerebral palsy as when such findings were not present.

Pneumoencephalography

The pneumoencephalogram is especially valuable when decisions must be made concerning the disposition of children who are severely handicapped. In these cases it is important to determine the presence and extent of cortical atrophy, since the prognosis is much better in cases of trauma to fully developed brains.[70, 102] When proper precautions are taken, it is a relatively safe procedure.[102-104] The most serious complication can be the accumulation of subdural fluid[105] and air emboli[106] after the procedure.

Cerebral Angiography

Another increasingly important diagnostic tool is cerebral angiography. Its prime value lies in the demonstration of vascular anomalies or aneurysms. The use of arteriography to clarify the causes of cerebral palsy in specific cases is possible. Levinson and Hartenstein[107] report a case of intracranial calcification following pneumococcal meningitis in which the clinical sequelae were generalized spasticity, rigidity, convulsions and mental retardation. Cerebral arteriography revealed thrombosis of the middle cerebral artery.

Electromyography

Electromyographic technics are becoming increasingly better standardized for utilization in diagnostic studies in cerebral palsy. Kugelberg[108] and Petersen,[109] using a special precise-timing method, have demonstrated that muscles supplied by diseased motor neurons have, on the average, action potentials of longer duration than normal.

Psychologic Tests and Audiometry

The use of these methods in diagnosis will be discussed in the sections on "Psychology" and "Habilitation."

Psychiatry

Psychiatric disturbances may be due to either emotional (psychogenic) factors or organic impair-

ment (involving various areas of the cerebrum). In spite of obvious organic damage in the child with cerebral palsy, both factors are frequently involved and must be considered in treatment.

The Organic Factor

Various authors have described a behavior syndrome that is characteristic of the child with brain damage. Rosenfeld and Bradley[110] have pointed out the following characteristics: unpredictable variability in mood; impulsiveness; short attention span; fluctuant ability to recall material previously learned; difficulty in learning arithmetic; and hyperactivity. Anoxia is thought to be the most important etiologic factor. Preston[63] and Stevenson,[111] who studied children suffering from paranatal or postnatal anoxia have found that the resulting behavior syndrome was often severe enough to be considered a serious handicap to future social adjustment. Developmental defects and encephalitis may be the cause of a similar behavior syndrome, as has been described by L. Bender and others.[112, 113]

The difficulties in patterning behavior are due to various factors.[112] Outstanding are the perceptual difficulties, which may be evaluated by psychologic testing (by such tests as the Bender Gestalt Test). Difficulties arising from motor and sensory impairment result in limitation of exploration of the outer world. Language difficulties further limit relations with the environment.

Psychogenic Factors

The recognition and treatment of emotional difficulties due to psychogenic factors should be considered as important as the correction of the motor impairment. The entire habilitation program is wasted unless the emotional needs and problems of the child are adequately met. Disturbances in the child's emotional life, psychosexual development and social experience are often the determining causes of behavior disorders and neurotic patterns of adjustment.

Psychoanalytic studies of the child with cerebral palsy reveal that such difficulties lead to prolonged infantile relations with the mother; this exaggerated dependency may hamper his exploration of the outer world and distort his approach to reality. Under stress these children have a greater tendency than normal children to regress to infantile patterns of behavior. These include passivity, diminished tolerance of frustration, persistence of strong needs and so forth.[114]

Schilder,[115] in a study of children with brain damage, concluded that unsolved motor problems in infancy may lead to later anxiety neurosis and may be connected with compulsive and obsessional features, and that the child's unconscious distortions of his own body image may lead to hostility toward himself and his parents.

Relation to Parents

The difficulties of the child with cerebral palsy are magnified by the attitudes of his parents and of society toward him. Menninger[116] has pointed out that society's reactions to the handicapped child are irrational and due to unrecognized elements of personality. Thus unconscious feelings of guilt, fear, hate or repulsion may be expressed as pity, oversolicitude, curiosity or rejection.

These attitudes and their unconscious motivations are especially important in the parent-child relation. The attitudes of the parents toward the crippled child are not always constructive. Nearly every parent is neurotically affected by his handicapped child. The child's defects may be unconsciously considered a punishment, and the resulting guilt feelings are transferred to the child. Self-condemnation and self-punitive fantasies occur in many such parents.[117] As a defense against these irrational, purely emotional feelings, the parents may react in various ways by showing: unwillingness to face the reality of the child's handicap, thus leading to exaggerated drives and ambitions that the child is unable to meet; overprotection, which limits the child's experience of the outer world and his striving for independence; rejection of the crippled child[118]; or an exhibitionistic attitude, with the child's achievements becoming a means of their own glorification.

These attitudes and unconscious reactions further handicap the child's adjustment. The crippled child has the same need of affection and love as the normal child. His strivings for independence, self-expression and identification with the adult are essential to normal personality development. Recent studies by Schwartz and others,[3] Grayson,[119] and Manson[120] have emphasized the importance of using the emotional needs of the patient to motivate him toward acceptance of the habilitation process.

The physician's attitude toward the parents of handicapped children has been discussed.[77] The parents must be assured that the child has had a careful, thorough examination by a conscientious physician who has not made his diagnosis in advance. Casual assurance that the child will "grow out of it" is misleading and may build up false hope and unrealistic attitudes. The physician should tell the parents the truth about their child and help them to face reality. On the one hand, he must understand the parents' reluctance to accept the diagnosis of cerebral palsy; on the other hand, the parents must learn to appreciate the implications of their child's handicap. The driving ambitions of the parents must be modified by the reality of the situation. Also, the child must learn to accept and to live with his handicap. This can be done only when parents have first learned to accept him. Individual or group psychotherapy with the parents and psychiatric interviews with the child[121, 122] are as important as

occupational and physical therapy and should be combined with it whenever possible.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

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CASE 37451

PRESENTATION OF CASE

First admission. A forty-seven-year-old man was admitted to the hospital because of inability to keep his eyes open.

Four years before entry the patient began to have difficulty in reading. An oculist found the left eye to be weaker than the right and prescribed glasses, which corrected his vision completely. About three years before admission he began to feel vaguely "not right," with fatigue, loss of energy and marked decrease in libido. He had been examined in another hospital two years before entry and found to be normal. His symptoms, however, gradually became worse. Ten months prior to entry he noted that the eyelids drooped, — especially the left, — and he had great difficulty in keeping his eyes open. At about this same time he began to experience weakness in the legs after walking moderate distances. During this period he also noted dyspnea on mild exertion and on flexing the neck sharply. The latter produced the sensation of "cutting off his wind." On two or three occasions during the last several months before admission he had attacks of diplopia while driving his car. Three months prior to entry a physician prescribed prostigmine, to be taken two to three times daily depending on the degree of the symptoms. These as well as weekly injections of a "nerve medicine" did not help him. Shortly before admission he had a constant feeling of fatigue and sleepiness and could walk only five or six blocks before he felt exhausted. He had also noted during this time a gradual falling out of hair of the scalp, axillas, trunk and pubic region. He had not been capable of sexual intercourse for two years. There had been no dysphagia, dysarthria or difficulty in swallowing or chewing.

The past history and systemic review were essentially negative.

Physical examination revealed a well developed and nourished middle-aged man with a large head and large features — a thick nose, thick lips and a protruding lower jaw. The skin was oily, coarse and peppered with sebaceous cysts; over the scalp it was in folds that resembled brain convolutions. The voice was deep toned, croaking, husky and weakened after exertion. The hair of the scalp was fine, thin and absent in irregular patches. The axillary hair was absent, that of the pubis almost so. There was a small amount of hair on the chest but none on the rest of the trunk. Ptosis and upper-lid weakness was more marked on the left; repeated opening and closing of the eyes resulted in slowed movements and finally inability to open the eyes. Vision was better in the right eye than in the left. The pupils reacted normally and the fundi were negative. There was a coarse nystagmus to the right. The bellies of the sternocleidomastoid muscles appeared enlarged bilaterally. The chest and abdomen were negative. The muscles of the extremities seemed of good strength initially but tired quickly. Tendon reflexes were sluggish. Vibration and position sense were normal.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 84 diastolic.

A urine specimen had a specific gravity of 1.010 and gave a + test for albumin; the sediment contained 10 red cells and a rare white cell per high-power field. Examination of the blood revealed a hemoglobin of 16.3 gm., a red-cell count of 5,000,000 and a white-cell count of 10,500, with 62 per cent neutrophils. A fasting blood sugar was 86 mg. per 100 cc. The serum sodium, chloride, cholesterol, calcium, phosphorus, phosphatase and potassium were normal. The sedimentation rate was 2 mm. in 60 minutes and a blood Hinton test was negative. A basal metabolic rate was — 4 per cent. Roentgenograms of the skull and chest were essentially negative. A lumbar puncture produced clear, colorless fluid under an initial pressure equivalent to 300 mm. of water with a drop to 287 mm. on removal of 2 cc. The spinal fluid contained 4 red cells and no white cells; the total protein was 20 mg. per 100 cc. A prostigmine test was negative. A biopsy of a neck muscle was reported as negative.

Second admission (approximately twenty-two months later). Two months before entry the patient began to note swelling of the ankles, which usually cleared up overnight but for the past six weeks had been constantly present. He had also noticed return of tiredness in the legs and dyspnea on exertion. There had been no orthopnea or palpitations. During the six months before entry he noted that his neck was growing larger and that he became short of breath on sudden neck flexion. There had also been a slight curling downward of the lower lip and a poor tolerance of his dentures.

Ptosis had increased slightly and ability to move the eyes from side to side had decreased. Loss of libido had persisted.

Physical examination was essentially as before, with the following added findings. The facies were more prognathic, with a scleroderma-like change in the skin beneath the lower lip and partial eversion of the lip (Fig. 1). The tongue and lips were large and thick. The striking finding was in the thyroid gland, which was diffusely stony-hard and enlarged to two or three times normal size. The lobes were not distorted, and there was no nodularity. The

FIGURE 1.

left border of the heart was 11 cm. to the left of the midsternum. There were no murmurs, and the aortic second sound was greater than the pulmonic. The liver edge was percussed one fingerbreadth below the right costal margin. The skin was generally hyperkeratotic and thickened, and the scalp was thickened and corrugated, as noted on the previous examination. The muscles showed no localized weakness, but the biceps, triceps and Achilles-tendon reflexes were absent. There was +++ ankle edema and ++ edema of the sacrum. An examination of the larynx revealed generalized slight thickening of the mucosa.

A neurologist found nearly complete external ophthalmoplegia, with slight movement, — possibly 10° to right and left and upwards and downwards, — and no convergence. The orbiculares oculorum and other facial muscles were normal, and there was probably some weakness of the skeletal muscles. There were no fibrillations, fasciculations or sensory changes.

The temperature was 98°F., the pulse 90 and the respirations 18. The blood pressure was 160 systolic, 105 diastolic.

A urine specimen had a specific gravity of 1.005 and gave a ++++ albumin. The sediment contained 25 red cells and 2 white cells per high-power field. There was no Bence–Jones protein. Four additional urines had specific gravities ranging from 1.008 to 1.012. A phenolsulfonphthalein test showed 8 per cent excretion in the first 15 minutes and 63 per cent at the end of two hours. The blood hemoglobin was 13.2 gm. and the white-cell count 11,300, with 69 per cent neutrophils. A blood smear was negative. The blood nonprotein nitrogen was 29 mg. and the total protein 4.6 gm. per 100 cc.; the sodium was 138.9 milliequiv., the potassium 5.4 milliequiv. and the chloride 106 milliequiv. per liter. The sedimentation rate was 14 mm. in 60 minutes. Radioactive iodine (I^{131}) was given by mouth as a tracer study; the patient excreted a normal amount, indicating normal thyroid function. The basal metabolic rate and electromyogram were normal. An electrocardiogram showed low voltage.

A roentgenogram of the chest showed slight narrowing of the trachea, with displacement to the left by an enlarged, nodular thyroid. There was a moderate amount of fluid in the right pleural cavity that rose to the level of the fifth rib in the axillary space. There was some increased prominence of the right hilus and a small amount of fluid in the left pleural cavity.

On the fifteenth hospital day an exploration of the neck was performed.

DIFFERENTIAL DIAGNOSIS

DR. ANDRIES QUERIDO*: Before I begin to discuss this very unusual case, I should like to see the roentgenograms.

DR. JOSEPH HANELIN: I have the films of the last admission here. Examination of the chest shows evidence of a moderate amount of pleural effusion on the right side and a small collection of fluid on the left side. The lungs themselves are clear. The vascular markings are prominent. The right hilus is prominent, apparently the result of vascular engorgement. I can discern no enlarged lymph nodes. In the lower portion of the neck there is a soft-tissue mass effecting a displacement of the trachea to the left. The report had it that this is a nodular thyroid, but this is in error. We are unable to demonstrate nodularity of the thyroid, and as far as I can tell from the films the entire gland is quite smooth. The heart is slightly enlarged in its transverse diameter and is larger than on the initial film, but there is no obvious asymmetrical increase in the size of the chambers.

DR. QUERIDO: Are there any roentgenograms of the hands?

DR. HANELIN: None were taken.

DR. QUERIDO: May I see the skull films?

DR. HANELIN: I do not have them here. They were quite normal. The pituitary fossa was normal.

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DR. QUERIDO: On what evidence was the diagnosis of prognathism made?

DR. HANELIN: That was a clinical diagnosis. We did not make it radiographically.

DR. QUERIDO: This forty-seven-year-old patient, who had apparently been well prior to six years before entry, developed, in the course of three years, difficulty with breathing, excessive fatigue, loss of ability to keep his eyes open and progressive weakness of the legs. Among the prominent symptoms was dyspnea. There was progressive weakness of the major muscle groups and the deep tendon reflexes apparently disappeared. There was a generalized loss of hair. During the second admission there was hypoproteinemia, a prominent proteinuria and, — very important, — a striking enlargement of the thyroid gland.

I should like to pull the initial symptoms apart, put them back together again and see what emerges. It is noted that this patient had large features — a large head, a thick nose, thick lips and a protruding lower jaw. The skin was so thrown into folds over the skull that an impression of brain convolutions was given. By the time of the second admission the prognathism had increased, as was indicated by the poor closure of his dentures. It is also stated that the tongue was large and thick. These features had not been present all his life but developed during the course of his illness. Acromegaly comes to mind to account for these features. There was no report in the protocol of the appearance of his hands or whether he had exostoses. These are not necessary for making a diagnosis of acromegaly, but in this disease both soft and bony tissues are affected. Sometimes the appearance of the skull is compared to that of a bulldog. The hypertrophy of the mucous membranes of the larynx also supports such a diagnosis. Against it, however, are the normal serum inorganic-phosphate figures. The serum phosphorus is generally, but not always, increased in acromegaly. Also counter to a diagnosis of acromegaly is the normal head size by x-ray examination, with a normal-appearing pituitary fossa. The first conclusion that I should like to make is that there is good reason to suspect that this patient had acromegaly.

One of the most striking features in this case was the large stony-hard thyroid gland. Nothing had been said about this in the other hospital four years previously. Yet at the time of the second admission the thyroid was two to three times enlarged and was a spectacular finding. I wonder if I can have more precise information about changes in the size of the thyroid between the two admissions here.

DR. EARLE M. CHAPMAN: The thyroid increased considerably in size between the two admissions. I think there was also a definite enlargement of the neck.

DR. QUERIDO: There is a certain amount of information available about the function of this thyroid. There was no clinical evidence of hypofunction, but there were enough symptoms of hypofunction to warrant concern. For this reason, presumably, a radioactive-iodine tolerance was done and it was found that a normal amount of the isotope was excreted. However, I think it is fair to question the interpretation of this result in this particular patient because of the generalized edema. I do not know just how this might affect the test and its interpretation, but one might wonder whether in the presence of edema the excretion of the radioactive iodine might be slower and thus in the usual forty-eight-hour specimen give a spuriously low result. Do we know the exact excretion figure?

A PHYSICIAN: Fifty-five per cent of the administered dose was excreted in forty-eight hours.

DR. QUERIDO: This means a retention of 45 per cent. It seems hardly likely that the edema could account for enough of the retained 45 per cent so that one could assume low thyroid function in the face of such a finding. Nevertheless I suppose I shall have to conclude that this gland was working normally.

There are three anatomic considerations that come to mind when one encounters a stony-hard thyroid gland: carcinoma of the thyroid, thyroiditis of the Riedel type and a calcified gland. It would be extremely difficult on clinical grounds alone to distinguish between these conditions. The time factor is not particularly helpful, nor is the estimate of thyroid function. A look at the periphery for metastases, however, would be valuable. Growth of carcinoma of the thyroid may be extremely slow and I think it is rare, or practically unheard of, to have hypothyroidism due to destruction of the thyroid by malignant disease. The finding of normal thyroid function might indeed slightly favor a diagnosis of cancer of the thyroid. The diffuse involvement of the gland, however, is somewhat against malignant disease. Thyroid disease in acromegaly is very common. Goiters are often found, and such patients are frequently hypermetabolic. In rare cases these patients fail to react to any form of thyroid therapy. Certainly, however, the thyroid findings recorded here are much more prominent than those encountered in the usual case of acromegaly. I am not sure the two conditions can be related in this case.

Apparently what brought the patient to the hospital was inability to keep his eyes open. This may or may not have been part of his generalized muscular disease. There was bilateral oculomotor palsy, with one side more accentuated than the other. There was not only involvement of the oculomotor system but also involvement of the other muscles, such as those of the leg and the sternomastoids. This suggests a generalized disorder of muscular function involving not only the eyes but other muscle groups as well. Therefore, we must consider some sort of neuromuscular disease. There were

never any sensory changes, so that whatever disorder, if neurologic, may have been present would have had to be localized in the anterior horn cells. The spinal-fluid examination showed no abnormalities of protein content or of cells; however, the pressure was high. The ocular fundi were normal and there were no signs of increased pressure. There was no muscular wasting, no fibrillation and no fasciculations, and a normal electrocardiogram was obtained. These findings suggest that the muscular picture must have been some kind of generalized muscular, rather than neurologic, disorder. I must say that I feel poorly prepared to discuss this phase of the problem. The patient was carefully studied for myasthenia gravis. Although one of the characteristic findings was present, the laboratory tests for this disorder were not convincing and there was an absence of dysphagia, dysarthria and difficulty in swallowing and chewing. Therefore, I do not see how a diagnosis of myasthenia gravis can be made.

In the literature there are reports of a true myopathy occurring in association with thyroid disease. The ophthalmoplegia, the acute nature of the disease and the periodic weakness are perhaps suggestive of thyrotoxicosis and indeed a clinical syndrome characterized by muscular weakness with severe periodic accentuation has been described in association with severe thyrotoxicosis. Such patients do not react at all to prostigmine. Further discussion of this point, however, is futile because all the evidence points away from an overactivity of the thyroid gland. This is objectively demonstrated by the normal radioactive-iodine tolerance test. This point should not be passed by, however, without mention of the hyperophthalmopathic type of Graves' disease in which the thyroid does not seem to be hyperfunctioning but in which there is considerable prominence of the eye features and oftentimes associated muscular weakness. These patients have severe proptosis, ophthalmoplegia, weakness of the levator palpebrae and oftentimes generalized weakness. Proptosis, however, is uniformly present and there was no evidence of proptosis here. The thyroid itself may be hyperfunctioning, functioning normally or even functioning at a subnormal level. I should like to ask Dr. Kubik at this point to comment on the muscular condition.

Dr. Charles S. Kubik: I have not had very much experience with myopathy associated with thyroid disease. The myopathy we have seen in thyroid disease has not been of such severe degree as is described in this case record. Perhaps Dr. Chapman can comment.

Dr. Earle M. Chapman: I do not believe that we have seen myopathy of this degree with thyroid disease.

Dr. Querido: I shall now go to other symptoms. At the second admission there was generalized edema, extreme hypoproteinemia with a total protein of 4.6 gm. per 100 cc. of serum and evidence of proteinuria. Serious malnutrition does not seem to be a possible cause for these findings. I think the proteinuria is sufficient explanation for he blood findings but what kind of renal disease was present in this patient? The blood pressure at the time of the first admission was 130 systolic, 84 diastolic, but by the time of the second admission it had risen to 160 systolic, 105 diastolic; this may be a very significant finding. The total phenolsulfonphthalein excretion was normal, but he only excreted 8 per cent in the first fifteen minutes. I do not attach much value to the total figure, but the 8 per cent figure may well be significant in that it indicates dilution of the dye. A concentration test is not reported but the highest concentration described is 1.012. This may well indicate some lowering of the concentrating power. The nonprotein nitrogen, however, was not elevated. Such proteinuria as is encountered here occurs mainly in four conditions: amyloid disease of the kidney, so-called lipoid nephrosis, chronic glomerular nephritis and Kimmelstiel–Wilson's syndrome, which is the type of glomerulosclerosis associated with diabetes. Was a Congo red test or a glucose-tolerance test done?

Dr. Tracy B. Mallory: A Congo red test was not done; a glucose-tolerance test was normal.

Dr. Querido: There are not many indications for amyloid disease although this diagnosis must be kept in mind in any condition where renal disease of long standing is present. My guess is that the kidney lesion is chronic glomerular nephritis or probably an intercapillary glomerular sclerosis. I am aware that speculations of etiology of kidney disease are very dangerous.

I am left with the fatigue, the loss of libido and the loss of the scalp hair to discuss. Decreased libido and fatigue can, of course, occur as part of any disease. Loss of pubic hair and axillary hair are found in Addison's disease in the female, myxedema and sometimes in thyrotoxicosis. Loss of hair can, of course, also be a primary ectodermal disease. Because the eyebrows are present in the photograph and the pubic hair was being lost in irregular patches, I should be more inclined to suspect a primary disease of the hair rather than some well defined systemic disorder. The skin became hyperkeratotic, such as often occurs in myxedema. I cannot with certainty link up the hair changes with any endocrine disorder such as acromegaly. Another point to be noted is the low voltage seen in the electrocardiogram. This is often encountered in myxedema but also in any condition where there is any considerable degree of peripheral edema and in scleroderma.

In short, I must say that I am unable to arrive at any wholly satisfactory explanation for the clinical picture presented by this patient. One might wonder whether he had not had a long siege of hyper-

thyroidism with fibrosis of the thyroid gland and whether this might account for the muscular disease. There is insufficient evidence, however, to make such a diagnosis. Is there any systemic or metastatic disease that could account for this picture? There are reports on amyloid disease of the thyroid*; however, a stony hard consistence is not present in those cases and seems, therefore, unlikely in this case. Doing what I can with the findings here, I should like to make a diagnosis of acromegaly and Riedel's thyroiditis and an undefined muscular disease with a renal lesion of the Kimmelstiel–Wilson type.

A PHYSICIAN: How much bleeding did he have at the time of the last biopsy or at the time of the operation?

DR. MALLORY: I think no abnormal amount.

DR. QUERIDO: Dr. Dobyns, can you say that the thyroid was truly hard?

DR. BROWN M. DOBYNS: It was very hard. It was removed in its original shape and was solid and hard.

DR. WALTER BAUER: I think you are on somewhat dangerous ground to make a diagnosis of Kimmelstiel-Wilson's disease. I should think you would need to have a hyperglycemia. Furthermore, I think the edema described here is not in keeping with that syndrome. I might say that a patient was recently sent here from Mt. Sinai Hospital who had amyloid disease of the thyroid gland. I cannot say that his was stony hard, but I can say that it was very much harder than the usual thyroid.

DR. DOBYNS: Dr. Bauer has raised the question of amyloid disease of the thyroid. I do not think I would have called this gland stony hard but it was certainly very hard.

DR. MALLORY: I should like to call attention to the lower jaw (Fig. 1). It does not look too big, and I think this would argue against acromegaly.

DR. QUERIDO: Well, the question is whether it was a soft-tissue rather than a bony process. The case hinges on this point to a large degree.

CLINICAL DIAGNOSIS

Nontoxic goiter with tracheal compression.

DR. QUERIDO'S DIAGNOSES

Acromegaly.
Chronic thyroiditis, Riedel type.
Undefined muscular disease.
Intercapillary glomerulosclerosis.

ANATOMICAL DIAGNOSIS

Primary systemic amyloidosis, generalized.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This thyroid was explored. Dr. Dobyns has told you what it looked and felt like at operation. The histologic examination showed a diffuse infiltration with amyloid. This differed from the case Dr. Bauer has mentioned in which amyloid was also proved; it was associated with large amounts of fat tissue. In this case no fat was present. Following that finding a biopsy was taken of the skin of the lip, and that was found also to be highly infiltrated with amyloid. The patient left the hospital and died about a year later. Practically nothing was known of his final course, but we did have an autopsy.

The gross findings were not very striking in the internal organs. The heart was somewhat large, weighing 440 gm., and the kidneys were enlarged, just over 400 gm. The liver and spleen were both small. The pituitary was grossly of normal size. Microscopical examination of the various organs showed that almost every part of the body was involved in one way or another with an amyloid process. That was very striking in the pituitary, which showed atrophy of parenchymal elements and a very marked amyloid infiltration in the interstitial tissues. In every organ amyloid was present in the walls of the blood vessels. This was especially prominent in the liver where, unlike the usual deposition in the walls of the sinusoids with resultant narrowing of the liver cords seen in secondary amyloidosis, amyloid was present only in the walls of the larger vessels (Fig. 2). There was extensive cardiac involvement, sometimes in the form of

FIGURE 2. *Photomicrograph of Section of Liver, Showing Amyloid Infiltration of Walls of Blood Vessels in Portal Space. Note absence of amyloid in walls of sinusoids.*

*Walker, G. A. Amyloid goiter. *Surg., Gynec. & Obst.* 75:374-378, 1942.

dense masses in the interstitial tissues and epicardium but often with replacement of muscle fibers. The large tongue and the ptosis can be explained by the extensive muscle involvement with amyloid (Fig. 3). The skin involvement accounted for the falling out of the hair. The kidneys showed amyloid-

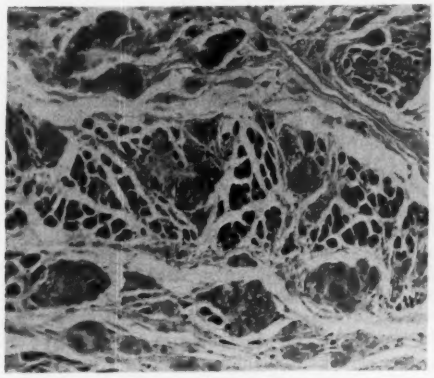

FIGURE 3. *Photomicrograph of Section of Tongue, Showing Pale-Staining Amyloid Infiltration Replacing the Darker-Staining Muscle Bundles.*

osis not only of the larger vessels but of glomeruli, tubules and interstitial tissues similar to the secondary form; the spleen showed only large-vessel involvement. The renal involvement was so extensive that it is possible that death was due to renal failure.

CASE 37452

PRESENTATION OF CASE

First admission. A fifty-seven-year-old woman was admitted to the hospital because of hemoptysis of five months' duration.

For the four years before admission the patient had a mild chronic cough productive of about half a cup of clear or yellowish sputum each day. For one-and-a-half years she had had episodes of exertional dyspnea, which had disappeared following digitalization and limitation of activity six months previously. A nasal cauterization was performed for sinusitis five months before admission. Shortly after this she began to raise quantities of dark-red sputum that would well up in her trachea. This was unaccompanied by pain or cough and persisted up to admission. She had no fever, pain or weight loss.

At the age of eight she had had typhoid fever and rheumatic fever, and at the age of twenty "Bright's disease." Up until four years before admission periodic episodes of painless jaundice had occurred, which had been ascribed by her physician to "hemolytic crises." One daughter also had (?) attacks of jaundice.

On physical examination the heart was enlarged 1 cm. beyond the midclavicular line. There was a harsh Grade III aortic systolic murmur transmitted over the entire chest. The aortic second sound was absent. The liver and spleen, which were palpable just below the costal margin, were slightly tender. The lungs showed questionable dullness at the left base.

The temperature was 96°F., the pulse 98, the respirations 20 and the blood pressure 125 systolic, 85 diastolic.

Urinalysis was negative. The hemoglobin was 11.8 gm. and the white-cell count 7600 with a normal differential; the red cells were normocytic and normochromic with a few target forms. The blood Hinton test was negative. The sedimentation rate was 3 mm. per hour and the prothrombin time 23 seconds (normal, 17 seconds). The nonprotein nitrogen was 35 mg. and the bilirubin 0.5 mg. direct, 1.1 mg. total per 100 cc. The red cells did not hemolyze in 0.5 per cent saline. No acid-fast bacilli were found in the sputum. An x-ray film of the chest showed accentuated vascular markings bilaterally and cardiac enlargement involving mainly the left ventricle. Bronchoscopy revealed mucosal bleeding in the left main bronchus. There was no evidence of intrinsic tumor, but at the level of the upper-lobe opening this bronchus was narrowed to one third its normal size by extrinsic pressure.

The patient was discharged after seven days in the hospital, on digitalis therapy.

Second admission (ten months later). In the interval the hemoptysis persisted. The patient had three additional attacks of syncope following exertion that were accompanied by urinary incontinence and nausea. She had noted a slight increase in dyspnea and a choking, constricting sensation under the sternum. These were not affected by change of position. Her doctor gave her one-fourth grain of morphine, 1/100 grain of nitroglycerin, 1 cc. of Mercuhydrin and oxygen by mask, applied tourniquets and sent her into the hospital.

Physical examination revealed a woman who was moderately dyspneic in the upright position. She was not cyanotic and appeared to be only moderately uncomfortable. The neck veins were flat. There were coarse moist rales bilaterally in the chest and dullness at both bases. Findings in the heart and abdomen were as at the first admission.

Examination of the blood disclosed a hemoglobin of 12 gm. On smear the red cells were generally normocytic and normochromic, with a few target forms; there were many spherocytes and slight anisocytosis and poikilocytosis. The reticulocytes were

7.4 per cent, the platelets abundant and the white cells normal. The bilirubin was 0.7 mg. direct, 1.1 mg. total per 100 cc. The hematocrit was 37 mm. and the prothrombin time 21 seconds (normal, 17 seconds). A Coombs test was negative. An x-ray film of the chest was unchanged from the previous admission.

She responded well to the routine measures instigated before admission and was discharged after eleven days' hospitalization on digitalis, nitroglycerin and a low-salt diet.

Third admission (two months later). In the interval she had been fairly well. Exertional dyspnea had curtailed her activity and she had an occasional brief episode of chest pain. There had been no hemoptysis. Two days before admission she felt extremely weak. The day of admission, following slightly more than usual activity, she became extremely short of breath.

The findings were similar to those of the second admission except that the blood pressure was 94 systolic, 70 diastolic, the nonprotein nitrogen 53 mg. per 100 cc. and the white-cell count 13,400 with 85 per cent neutrophils. An electrocardiogram showed sinus tachycardia at a rate of 140, left-axis deviation, rather high R waves in Leads 1, V_5 and V_6 and deeply inverted T waves in Leads 1, 2, AVL, V_4 and V_6.

She was treated with oxygen, tourniquets, digitoxin and Mercuhydrin. She improved rapidly and was discharged after six days.

Final admission (two months later). In the interval at home she had led a bed-to-chair existence. Four weeks after discharge she became anorexic, with marked weakness, nervousness and insomnia. The abdomen became swollen three weeks before entry. She was treated with digitoxin, phenobarbital and mercurial diuretics, but in spite of this the urinary output declined. Four days before admission edema of the lower extremities made its appearance. Dyspnea had not increased in severity and there were no episodes of chest pain.

Physical examination revealed a cachectic, chronically ill woman. The heart was much larger than at previous admissions. There was a gallop rhythm at a rate of 100. The heart sounds were very distant and only a faint systolic murmur could be heard in the aortic region. A Grade II to III systolic murmur was audible over the tip of the sternum and a questionable systolic murmur was present at the apex. The aortic second sound was almost inaudible and the pulmonic second sound was accentuated. The blood pressure was 80 systolic, 65 diastolic, but the sounds were barely audible. A few rales were heard over the lungs, which were dull at the bases. The abdomen was distended and had a fluid wave. The liver was tender and its lower edge was 10 cm. below the costal margin. There was sacral and pretibial edema. The neck veins were distended.

The temperature was 100°F., the pulse 62 and the respirations 28.

The urine had a specific gravity of 1.010 and gave a +++ test for albumin and a + test for bile; the sediment contained an occasional red cell and white cell and many granular, hyaline and cellular casts. Examination of the blood revealed a hemoglobin of 13 gm. and a white-cell count of 14,300 with 96 per cent neutrophils. The total protein was 5.8 gm., the nonprotein nitrogen 92 mg. per 100 cc.; the carbon dioxide was 22 milliequiv. and the chloride 87 milliequiv. per liter. The prothrombin time was 26 seconds (normal, 19 seconds), and the bromsulfalein retention 34 per cent. The x-ray film of the chest showed the transverse diameter of the heart to be increased in size over the previous examinations. There was a generous amount of fluid in the right pleural cavity and probably a considerable amount in the left. Pulmonary vascular channels were engorged. There were mottled and conglomerate densities throughout both peripheral lung fields, particularly in the lower portions. In a second film a small area of density was noted over the right diaphragm. The electrocardiogram was similar to previous tracings except for minor variances in the ST and T-wave changes.

Throughout the hospital stay the patient's output was very low, being approximately 200 cc. per day. She was restless and uncomfortable, deteriorated rapidly and died on the third hospital day.

Differential Diagnosis

Dr. Victor G. Balboni*: This woman was first admitted to the hospital for study because of hemoptysis. There was no evidence of intrinsic tumor at bronchoscopy, but there was narrowing at the level of the upper-lobe bronchus on the left as if by extrinsic pressure. The mucosa of the bronchus was said to be bleeding, but no adequate cause for the bleeding was found. Physical examination revealed severe aortic stenosis, which I presume was on the basis of the rheumatic fever she had had in childhood.

May I see the x-ray films that were taken during the first admission?

Dr. Milford D. Schulz: In the x-ray films of the chest, the heart is enlarged principally in the region of the left ventricle. One film was overexposed in an attempt to show calcification in the region of the valve, but it was not observed. There is slight engorgement of the pulmonary vessels. The spleen is considerably enlarged. The liver appears about normal in size.

Dr. Balboni: The chronic cough and the raising of half a cup of sputum daily are consistent with bronchiectasis. Why should a woman of fifty-seven develop bronchiectasis? Bronchiectasis often develops distal to an area of bronchostenosis. Since on bronchoscopic examination there was nothing

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wrong with the inside of the bronchus and there was a suggestion of extrinsic pressure without any other obvious disease of the lung or mediastinum to cause it, I wonder whether the heart could have been sufficiently enlarged to compress the bronchus. Dr. Schulz, can an enlarged heart cause pressure on the left bronchus?

DR. SCHULZ: An enlarged left auricle can cause obstruction to the bronchus.

DR. BALBONI: At the point where the left-upper-lobe bronchus branches from the main bronchus?

DR. SCHULZ: At about that level.

DR. BALBONI: Of course, it is not uncommon for bronchiectasis to develop in patients of this age following severe virus pneumonia or a pneumonia that does not resolve completely.

During the second admission the patient had the characteristic picture of left-ventricular failure. On the third admission, when she was again in heart failure, the systolic blood pressure had dropped so the pulse pressure was flat — 94 systolic, 70 diastolic — a characteristic finding in patients with left-ventricular failure. The changes in the electrocardiogram were more or less consistent with an enlarged ventricle.

A few days before the final admission the patient became progressively more edematous, but the dyspnea did not increase. In the presence of right heart failure, acute pulmonary congestion may be somewhat relieved; it is possible that is what happened here. On examination there was fluid in the abdomen and in the lungs. The urine, which had been negative on the first admission and was not mentioned on the other two admissions, contained +++ albumin, + bile and many hyaline casts. That the urine during the first admission was normal indicates to me that whatever was going on in the kidneys was not related to the Bright's disease of childhood. These changes in the urine may be explained on the basis of either the heart failure or some other condition. We know that in heart failure there may be marked albuminuria; in the presence of albumin there may be casts, so I think the heart failure alone can explain it. The bile may have been due to hemolysis of blood or to primary liver damage. The hemoglobin of 13 gm. is against any significant amount of hemolysis and the bilirubinuria suggests liver disease.

At the time of the first admission, a history of hemolytic crises was elicited and various tests were done. The van den Bergh was above normal, but the red cells did not hemolyze in 0.5 per cent saline as they do in most patients with congenital hemolytic jaundice. On the second admission the reticulocyte count was high and in the peripheral blood there were spherocytes; these findings are quite consistent with congenital hemolytic jaundice. A Coombs test was negative, which is also consistent with congenital hemolytic jaundice. The Coombs test helps to differentiate congenital hemolytic jaundice and acquired hemolytic jaundice. It is advantageous to know which type is present because splenectomy cures congenital hemolytic jaundice but usually is not helpful in acquired hemolytic jaundice. The patient's daughter had congenital hemolytic jaundice and I believe the patient also had it.

May I see the x-ray films of the final admission now?

DR. SCHULZ: In the film made ten months to a year after those of the first admission, the aortic shadow is increased somewhat; the engorgement of the lung roots has not increased much. Four months later the heart is quite large and the pulmonary engorgement is considerable. The lungs are edematous and there is fluid in the pleural sinus.

DR. BALBONI: The protocol mentioned an area of density above the right diaphragm.

DR. SCHULZ: That may be due to fluid in the interlobar septum, or I suppose pneumonia or infarction.

DR. BALBONI: This looks like pulmonary congestion. Certainly in heart failure large areas of pulmonary edema may show up as conglomerate areas.

DR. SCHULZ: It can all be explained on the basis of pulmonary congestion and cardiac failure.

DR. BALBONI: It is hard for me to explain all the findings in this case. It seems to me that rheumatic valvular heart disease and chronic congestive failure explain most of the symptoms. There were three or four episodes of acute pulmonary edema followed later by right-sided heart failure, congestion of the liver, enlargement of the liver, ascites and peripheral edema. All these findings could be explained on the basis of severe dropsy due to heart failure, and I think that is what she had. She also must have had some pulmonary disease, — presumably bronchiectasis, — to produce the large amount of sputum she was raising. Patients with bronchiectasis do bleed, but they do not bleed as much as this woman did. I think I have to search for some other explanation for the bleeding. Could it have been due to increased pressure in the pulmonary vessels because of the left-sided heart failure? We know that patients with mitral stenosis bleed.

The degree of liver failure, — 35 per cent retention of bromsulfalein, — is rather unusual for heart failure alone and makes me wonder whether some primary liver disease was present. I accept the periodic episodes of jaundice as congenital hemolytic jaundice, but I am not aware that it has ever caused severe liver disease. The episodes of hemolysis may give rise to pigment stones in the gall bladder, and as a result of the stones an ascending cholangitis and eventually a chronic biliary cirrhosis may develop. There was nothing in the history, however, to suggest it — no chills or fever.

Subacute bacterial endocarditis is not an uncommon complication in aortic valvular disease. Could

this patient have developed it? Systolic murmurs were heard at the base, in the mitral area and over the tricuspid area. These most probably are on the basis of acute cardiac dilatations but also may have been due to bacterial endocarditis. She had a low-grade fever on the last admission, and here again fever is not uncommon in heart failure, although it also raises the question of a terminal subacute bacterial endocarditis. The spleen was enlarged originally, as it usually is in congenital hemolytic jaundice, so that its enlargement does not help in the differential diagnosis of subacute bacterial endocarditis in this case. I do not believe there is enough evidence to say definitely that she had subacute bacterial endocarditis.

My diagnoses are aortic stenosis with congestive heart failure, congenital hemolytic jaundice and some degree of bronchiectasis perhaps due to pressure on a bronchus by an enlarged heart. I shall raise the questions whether she may also have had biliary cirrhosis as a complication of hemolytic jaundice and whether she may have had a terminal subacute bacterial endocarditis.

Clinical Diagnoses

Acute congestive failure.
Aortic stenosis.
Rheumatic heart disease.
?Neoplasm.

Dr. Balboni's Diagnoses

Aortic stenosis with congestive heart failure.
Congenital hemolytic jaundice.
Bronchiectasis.
?Biliary cirrhosis.
?Subacute bacterial endocarditis, terminal.

Anatomical Diagnoses

Rheumatic heart disease with aortic stenosis.
Mural thrombi, right auricular appendage and left ventricle.
Pulmonary infarcts, old, left lung and right lower lobe.
Renal infarcts, old, bilateral.
Congenital hemolytic jaundice.

Pathological Discussion

Dr. Austin L. Vickery: This woman had an enlarged heart weighing 510 gm. The hypertrophy was primarily left sided, with the right showing no enlargement except dilatation. The valves, except for the aortic valve, were quite normal. The aortic valve showed an extreme degree of thickening of the individual cusps, calcification extending throughout the entire substance and interadherence of the leaflets, which is quite characteristic of rheumatic endocarditis. An additional finding in the heart was the presence of organized mural thrombi in the right-auricular appendage and left-ventricular apex.

In the lungs there were multiple infarcts. Specifically, a 4-cm. infarct was present in the lingula of the left upper lobe. An embolus was lodged in the artery supplying that area. This was entirely adherent and old. In addition there were small infarcts — old, in the right lower lobe, — and one in the left lower lobe in the costophrenic angle that was hidden on the x-ray film by the pleural fluid. It was our interpretation that many of these smaller ones were old. I think that the hemoptysis that this woman had been having for a period of time may very well have been on the basis of small infarction episodes.

Dr. F. Dennette Adams: If she had bled for several days but not a large amount I would wonder if it was the cause of it.

Dr. Vickery: We also wondered whether that was the explanation. Our wonderment was augmented by the fact that we did not find any other explanation for the hemoptysis. We did not see any clear-cut evidence of bronchiectasis, and the bronchial tree looked all right. I certainly sympathize with Dr. Balboni in the bronchoscopic observation. What relation it had to the final picture I cannot tell you. From where did the pulmonary emboli come? No thrombosis was found in the deep veins of the legs, but there was extensive thrombosis of the pelvic plexus of veins. This process appeared to be more recent than did the organized thrombi in the right auricle; therefore, it seems more logical to assume that the episodes of pulmonary infarction originated from the right auricle. The liver was large and markedly congested — not cirrhotic. The spleen was about three times the normal size and microscopically showed the characteristic picture of congenital hemolytic jaundice, with the splenic pulp engorged with closely packed red cells. There were bilateral small renal infarctions, which undoubtedly emanated from the thrombi found in the left-ventricular apex. There is one thing I have not commented on in the description of the calcified and stenotic aortic valve: At the time of autopsy we saw small fibrin thrombi looking a great deal like vegetations on the aortic-valve cusp and were curious as to whether these might represent a terminal subacute bacterial endocarditis, as suggested by Dr. Balboni. It is not uncommon to find little aggregates of fibrin adherent to valve cusps; these are called marantic thrombi and apparently form in the agonal phase. That is what these appear to have been.

Dr. Adams: No signs of rheumatic myocarditis?

Dr. Vickery: No evidence of active myocarditis was found.

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ABUSE OF TRANSFUSION THERAPY

In the past ten years the rapid expansion of private blood banks and the introduction of the Red Cross blood programs have made blood available in large quantities. With this marked increase in supply has come a much greater use on the part of physicians. In many hospitals transfusion care has passed from a rarity into a common form of therapy. Although there can be no doubt that this has brought about a great improvement in patient care, rapidity of convalescence and safety in surgery, an abuse has also crept in, in the form of administration of transfusions when no real therapeutic indications exist. This abuse is largely manifested in so-called "cosmetic transfusions" — that is, blood given to patients with normal hemoglobins and red-cell counts merely in the hope it will make them feel better or to make them think something is being done for them, or because their relatives have deposited blood in the bank or for other similar reasons.

The three main objections to this abuse are on ethical grounds — the shortness of supply and the dangers of transfusion. The first of these requires little comment; the administration of blood without adequate clinical indication is as condemnable a practice as unnecessary surgery or uncalled-for medication. The shortness of supply is a serious problem of which all clinicians should be thoroughly aware. With Red Cross programs now widespread, the wasting of a pint of blood in one hospital means so much less for a patient who really needs it in another, so much less blood for our troops in Korea and so much less to go into plasma for the armed forces or for civil defense. Plasma reserves are very small, yet the point of maximum blood donation by the population is being rapidly reached. To have enough blood to cover present real needs physicians must carefully select for transfusion only those patients who really require blood.

With the increased use of blood, the hazards attendant on its use have to a great degree been lessened by better laboratory methods, better testing serums and an improved knowledge of transfusion reactions. Despite these improvements, new hazards are constantly appearing. Hemolytic reactions are far from uncommon. Percentage-wise they are less, but their actual number is greater each year, largely because of errors in labeling, confusion of pilot tubes, lack of observation of the patient during transfusions and so forth. Furthermore, as more patients are receiving transfusions, more and more are becoming sensitized to blood subgroups and the rarer blood groups, introducing a new peril in the form of the sensitized patient. Homologous serum hepatitis is as real a danger as ever, coming as it does from donors who are carriers or who are in the incubation period of the disease, for the virus is still undetectable by laboratory methods. It causes an appreciable morbidity rate, and a mortality rate reported as high as 1 for every 6000 whole-blood transfusions. Infected

blood causes the death of a few patients each year. Lastly, other transfusion reactions, which vary from a fraction of 1 per cent to as high as 10 per cent in some hospitals, cause considerable discomfort and even complications in some patients. The mortality rate from transfusion is higher than that of appendicitis or of ether anesthesia.

With these facts in mind, it is well for all physicians to consider carefully whether a transfusion is clearly indicated before ordering it for a patient.

PREPROFESSIONAL EDUCATION FOR MEDICINE

Most physicians know that a very comprehensive examination of all medical schools is under way in the Survey of Medical Education now being conducted by the American Medical Association. Not so many realize that at the same time a subcommittee of seasoned educators has been reviewing preprofessional education. The objectives of this subcommittee were decided on at the outset: to determine the qualifications a student should possess to progress to a successful medical career; to ascertain in terms of student selection, guidance and education the extent to which undergraduate colleges are providing the kind of students the medical schools want; and to prepare as detailed a report as possible on the basis of this investigation.

The committee has considered very seriously the matter of fitness for medical training and has proposed as a yardstick the following characteristics: sterling character, sound motives for wishing to enter medicine as a career, a balanced education, emotional stability, promise of growth, academic fitness and adaptability.

In order to obtain the necessary information about premedical institutions a personal visitation was deemed essential. It was obviously impossible to visit every single school, and a nationwide sampling was accordingly planned to include large, small, state-operated, endowed colleges and so forth. A list was made up of 100 colleges over the country that had prepared five or more premedical students a year. From three to five days were spent at each institution. At each one not only were the administrators, premedical advisers and other faculty members interviewed, but the members of the committee also visited classes, talked with students and admissions officers and inspected student programs. A fifteen-page report was prepared on each institution with regard to many details of the educational program, extracurricular activities, characteristics of the student body and discipline. The advisory system in each college was of special interest in regard to the details of the system, the relation of the college itself to the premedical program, the areas of advising by the premedical adviser, the relation of the premedical adviser to the students and the relation of the premedical adviser to the medical schools.

The committee has indicated, in a recent preliminary report,* that certain generalizations are warranted, although it expresses the opinion that further investigation of the other schools may alter its final report. It has found a lack of institutional objective, departmentalization and overspecialization, lack of a balanced education, poor or mediocre instruction, lack of facility of communication among students as evidenced by their inability to read rapidly and to express themselves clearly and logically in speech and writing, too much lecturing and too little active participation of the student in the learning process and poor premedical guidance.

These generalizations are a severe indictment of premedical training. However, the committee has undoubtedly observed institutions with excellent instruction and an absence of the faults it has described and has noted many institutions that only have some of these deficiencies. The mere fact that thus far in its survey this committee of educators has found it necessary to paint such a pessimistic picture with these general statements would almost make it seem that the present and past generations of physicians have overcome quite a handicap to have contributed as much as they have done toward the comfort and well-being of their patients and to the progress of modern medicine. There can be no doubt, however, that the final report of such a survey of premedical education will contribute greatly to the selection of more capable students and the more adequate training of students preparing for medicine.

*Carman, H. J. Preprofessional survey of medical education: progress report. *J. A. M. A.* **146**:81-85, 1951.

OLD BOOKS: NEW LIBRARIES

TWELVE years ago, members of the Academy of Medicine of Toledo and Lucas County, Ohio, dreamed of a medical library. Next summer, thirteen years later, a $235,000 building with an ultimate capacity of 35,000 volumes will realize that dream; its construction is already under way.

This library not only will be a repository for books but will house a telephone service bureau that is expected to be of vital importance to Toledo's civil-defense organization in the event of an emergency. It will be the nerve center through which medical assistance is located and dispatched. The building will contain an auditorium for medical meetings and seminars, conference rooms and a lounge.

Toledo is not a teaching center. There is no medical school in the Toledo area. But the physicians of northwestern Ohio fully realize the necessity for a community medical library, and the 467 members of the Toledo and Lucas County Academy are to be congratulated for having inaugurated and successfully completed their fund-raising campaign.

The Boston Medical Library was similarly founded, in 1900, by eager, forward-looking physicians of this community. Enlarged thirty years later, it now houses 212,000 volumes, including the finest collection of incunabula in any medical library in the country, in addition to 150,000 pamphlets and dissertations. But it houses them in, around, on top of and under stacks built to accommodate some 75,000 volumes. Many are piled in old boxes in the basement.

The Boston Medical Library has about 1000 paying fellows, and the 6000 members of the Massachusetts Medical Society participate in all its benefits in return for only $5.00 a year. The Library is struggling to make ends meet. Its equipment and facilities are more quaint than efficient. Director James Ballard has done an incomparably brilliant job in holding the place together, bibliothetically and managerially, with baling wire and string. Mr. Ballard, however, is a veteran of sixty years' service; when he retires, it will be difficult to find one who can or will carry on his activities.

The Boston Medical Library has a great deal to offer the medical community and the community at large. It deserves support — not in tiny five-dollar contributions (although it needs these desperately) but in tens or hundreds of thousands of dollars.

Lucas County's achievement should arouse hope and confidence that something equally creditable can be done in Massachusetts to bring its own splendid library up to date.

CRIME DETECTION AT HARVARD

ERLE STANLEY GARDNER, the well known writer of mystery stories, creator of Perry Mason and Della Street, pays an outstanding tribute to the Department of Legal Medicine of the Harvard Medical School, its faculty and Mrs. Frances G. Lee in the foreword of his story *The Case of the One-Eyed Witness*, published in 1950. Mrs. Lee, now a captain in the New Hampshire State Police, has long been interested in crime detection and was originally impressed by the extraordinary talents of the late Dr. George Burgess Magrath, medical examiner of Suffolk County, Massachusetts, comprising much of the City of Boston.

She endowed the professorship of legal medicine at Harvard in his name and gathered together, with the assistance of James F. Ballard, director of the Boston Medical Library, a collection of periodicals to form the nucleus of a good collection on legal medicine. Dr. Magrath was the first occupant of the chair of legal medicine and was followed by the equally capable Dr. Alan R. Moritz, now at Western Reserve University.

Semiannually there is held at Harvard Medical School, under the auspices of Captain Lee, an intensive seminar on crime detection. Eight or ten of the outstanding experts in this field conduct a one-week course, for a class of about twenty-five especially selected state police officers, on everything pertaining to murder, from detection to an actual post-mortem examination.

One of the recent guest instructors in this seminar was Dr. Robert P. Brittain, a young lawyer and doctor of medicine, of Leeds University, Leeds, England, an outstanding leader in forensic medicine, to whom Mr. Gardner dedicated his previously mentioned book.

Correspondents very naturally wish to know what success attends the efforts making in Boston for the education of idiots. The institution is in its infancy, but making good and satisfactory progress.

Boston M. & S. J., *November 12, 1851*

OBITUARY

ALBERT EHRENFRIED
1880–1951

Dr. Albert Ehrenfried, who died on September 25, 1951, was born in Lewiston, Maine, on February 9, 1880. He graduated from Harvard College in 1902 and from Harvard Medical School in 1905, after which he had a distinguished career as visiting surgeon to the Boston City Hospital, the Children's Hospital, the Beth Israel and several other Boston hospitals. He was a member of the Faculty of Harvard Medical School and the Harvard Graduate School of Medicine, teaching anatomy and clinical surgery. He was an instructor of army surgeons during World War I.

Dr. Ehrenfried made many original contributions to surgery, his published works covering a wide field. He was a co-author, with Dr. L. R. G. Crandon, of *Aftertreatment of Surgical Cases*, published in 1909, and was editor and translator of *Krause–Heymann–Ehrenfried's Surgical Operations*, which appeared in 1915, and author of many original articles. In conjunction with Dr. F. J. Cotton he reintroduced in America the Reverdin or pinpoint method of skin grafting in 1909 and established in the same year the nonoperative method of treating clubfoot in infants and children. In 1911 he demonstrated that a saturated aqueous solution of picric acid possessed definite advantages as a dressing for burns and developed a technic for end-to-end arterial anastomosis with Dr. W. M. Boothby. He devised an apparatus for the administration of ether in anesthesia by intratracheal insufflation in the same year, and described a congenital distortion of the foot to which he gave the name of potential calcaneovalgus in 1914. He reported an uncommon skeletal growth distortion to which he gave the name of hereditary deforming chondrodysplasia in 1915. He was the first in New England, in 1932, to present a series of cases subjected to phrenicectomy in the treatment of tuberculosis.

Dr. Ehrenfried gave, in addition, considerable time and effort to constructive civic works. He held various offices in local and state medical societies, as well as in nonmedical institutions and organizations. He was a member of the examining committee of the Boston Public Library, a trustee of the Boston Medical Library, a fellow of the American Association for the Advancement of Science and of the American College of Surgeons, a councilor of the Massachusetts Medical Society, a member of the American Genetics Association, the American Eugenics Association, the Bostonian Society, the American Jewish Committee, Phi Rho Sigma and Tau Epsilon Phi and president of the Norwood Medical Society. He was an honorary life-president of Temple Sinai and a member of its board of trustees.

S. K.

MASSACHUSETTS MEDICAL SOCIETY

AMERICAN MEDICAL ASSOCIATION MEMBERSHIP AND FELLOWSHIP

This question-and-answer explanation of the American Medical Association dues problem is divided into two sections.

PRIOR TO 1950

Q. How did one become a member of the American Medical Association?

A. By becoming a member of a district society one became a member of the state society and the American Medical Association.

Q. Were there any American Medical Association membership dues?

A. No.

Q. Did a member receive the *Journal of the American Medical Association?*

A. No.

Q. How did one receive the *Journal of the American Medical Association?*

A. By becoming a Fellow of the American Medical Association and paying the subscription rate, whatever it was at that time.

Q. Were there dues in 1949?

A. No. There was a voluntary assessment of $25.00.

AFTER 1949

Q. Are there now membership dues?

A. Yes. They are $25.00 per year.

Q. Are they compulsory?

A. Yes.

Q. How does one receive the *Journal of the American Medical Association?*

A. In 1950 the subscription rate was $12.00, in addition to the membership dues.

In 1951 the membership dues of $25.00 will include the subscription to the *Journal of the American Medical Association.*

If a member does not wish to receive the *Journal of the American Medical Association*, he may have substituted one of the specialty journals published by the Association.

Q. Can one expect to pay 1951 dues and skip 1950 dues and remain a member?

A. No. If you belonged to your state society prior to January 1, 1951, you must pay 1950 dues

first. Checks will not be applied toward delinquent 1950 American Medical Association dues without your permission.

Q. How may one avoid paying American Medical Association dues if he is still an active dues-paying member of the state society?

A. Only by resigning from the Association.

Q. Does status in the American Medical Association affect membership in the Massachusetts Medical Society?

A. No.

Q. What are the fellowship dues for 1951?

A. $5.00.

Q. How do I obtain fellowship?

A. A dues-paying active member is eligible for fellowship and may request such status by applying directly to the secretary of the American Medical Association. Fellowship dues are payable directly to the Association on receipt of the bill for such dues.

Q. Why become a fellow?

A. A Fellow can read and discuss papers before the scientific assembly, hold office in the American Medical Association and be a delegate to it. Members do not have these privileges.

Q. Who is exempt from payment of the American Medical Association dues?

A. An active member of the Association may be excused from the payment of membership dues provided that he is excused from the payment of part or all of his state-society dues. Such members include: Fellows in active service in the armed forces; interns; residents; any physician over seventy years of age even though an active member of the state society; those retired from the society at the age of sixty-five; and those excused by the state society because of financial hardship.

Q. Is there any hope that this situation concerning fellowship and membership will be clarified?

A. Yes. Steps are being taken to change the by-laws of the Association to provide for one classification of membership carrying all privileges.

H. Quimby Gallupe, M.D., *Secretary*

DEATHS

Aycock — William L. Aycock, M.D., of Brookline, died on October 24. He was in his sixty-fourth year.

Dr. Aycock, who received his degree from the University of Louisiana School of Medicine in 1914, was for twenty-three years associate professor of preventive medicine and hygiene at Harvard Medical School and the Harvard School of Public Health. He was a fellow of the American Medical Association, a member of the American Public Health Association and the American Society of Bacteriologists and a former president of the American Epidemiological Society.

His widow and three daughters survive.

Crocker — Harvey J. Crocker, M.D., of Essex, died on September 7. He was in his thirty-fifth year.

Dr. Crocker received his degree from Tufts College Medical School in 1942.

His widow, a daughter, two brothers and a sister survive.

Sheehan — Katharine C. Sheehan, M.D., of Salem, died on October 22. She was in her eighty-first year.

Dr. Sheehan received her degree from Tufts College Medical School in 1908.

A son and three daughters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1951

Résumé

Disease	September 1951	September 1950	Seven-Year Median
Chancroid	1	2	2
Chicken pox	87	106	110
Diphtheria	2	4	11
Dog bite	1050	957	942
Dysentery, bacillary	0	11	11
German measles	64	78	47
Gonorrhea	184	199	393
Granuloma inguinale	1	0	0
Lymphogranuloma venereum	1	2	1
Malaria	36	0	7
Measles	174	97	97
Meningitis, meningococcal	3	3	3
Meningitis, Pfeiffer-bacillus	2	2	1
Meningitis, pneumococcal	1	3	1
Meningitis, undetermined	6	2	2
Mumps	294	173	173
Poliomyelitis	68	188	162
Salmonellosis	11	10	10
Scarlet fever	53	92	130
Syphilis	156	91	206
Tuberculosis, pulmonary	165	185	200
Tuberculosis, other forms	9	8	14
Typhoid fever	2	1	1
Undulant fever	0	1	2
Whooping cough	191	285	463

Comment

The diseases notably above the seven-year median for September are German measles, malaria, measles and mumps. Most of these malaria cases were reported from military hospitals and represent relapses in men returning from Korea and other foreign areas.

Diseases below the seven-year median for this month are diphtheria, bacillary dysentery, poliomyelitis, scarlet fever, undulant fever and whooping cough.

The 294 cases of mumps represent the second highest number ever reported for this month in this state.

The 68 cases of poliomyelitis for September are significantly fewer than August's 94 cases, indicating that the peak of this year's poliomyelitis season is past.

The number of cases of diphtheria, scarlet fever and whooping cough is the lowest incidence of these diseases ever reported in our records for this month.

This is the first year in which no cases of bacillary dysentery were reported for the month of September.

For five consecutive months no cases of undulant fever have been reported — a record for this disease.

Geographical Distribution of Certain Diseases September, 1951

Diphtheria was reported from: Boston, 1; Wilmington, 1; total, 2.

Dysentery, amebic, was reported from: Newton, 1.

Encephalitis, infectious, was reported from: Cohasset, 1; Foxboro, 1; Murphy Army Hospital, 1; Worcester, 1; total, 4.

Hepatitis, infectious, was reported from: Cambridge, 2; Greenfield, 1; Murphy Army Hospital, 1; total, 4.

Malaria was reported from: Dedham, 1; Murphy Army Hospital, 33; Walpole, 1; Waltham, 1; total, 36.

Meningitis, meningococcal, was reported from: New Bedford, 1; Springfield, 1; Taunton, 1; total, 3.

Meningitis, Pfeiffer-bacillus, was reported from: Fitchburg, 1; Hanson, 1; total, 2.

Meningitis, pneumococcal, was reported from: Weymouth, 1.

Meningitis, undetermined, was reported from: Boston, 1; Braintree, 1; Fall River, 1; Lynn, 1; Revere, 1; Shirley, 1; total, 6.

Poliomyelitis was reported from: Amesbury, 1; Amherst, 1; Arlington, 1; Ashland, 1; Ayer, 1; Belmont, 1; Boston, 18; Cambridge, 2; Cummington, 2; Everett, 1; Falmouth, 2;

Fitchburg, 1; Greenfield, 1; Groton, 1; Haverhill, 1; Hingham, 1; Hopkinton, 1; Hull, 1; Lawrence, 1; Leominster, 4; Lexington, 2; Malden, 2; Medford, 1; Newton, 2; Orange, 2; Pepperell, 1; Quincy, 1; Salem, 1; Springfield, 3; Sterling, 1; Swampscott, 1; Waltham, 2; Wellesley, 1; West Springfield, 1; Worcester, 4; total, 68.

Salmonellosis was reported from: Boston, 1; Brookline, 1; Hull, 1; Leominster, 1; New Bedford, 1; Rockland, 1; Salem, 1; Sharon, 2; Walpole, 1; Worcester, 1; total, 11.

Septic sore throat was reported from: Adams, 4; Boston, 1; Milton, 1; total, 6.

Trichinosis was reported from: Boston, 1; Murphy Army Hospital, 1; total, 2.

Tularemia was reported from: Chilmark, 1.

Typhoid fever was reported from: Dedham, 1; Worcester, 1; total, 2.

MISCELLANY

THE SOLDIERS' HOME IN HOLYOKE

The Soldiers' Home in Holyoke, rapidly nearing completion, is expected to be ready for occupancy soon after January 1, 1952. This 234-bed combination dormitory and hospital, constructed and maintained by the Commonwealth of Massachusetts, will offer the same type of medical service to Massachusetts veterans that is now being provided by the Soldiers' Home in Chelsea, Massachusetts, the Holyoke institution being primarily intended for veterans of the western section of Massachusetts. A temporary medical executive committee has recently been appointed to formulate medical policies for this new state veterans' facility. Resident medical-staff positions of medical intern, assistant physician and senior physician, at an annual salary, will be available soon after January 1, 1952. A visiting and consultant medical staff is being organized; all interested physicians, particularly those in the western section of Massachusetts, are invited to submit applications to the medical executive committee. It is planned to have 4 surgical and 4 medical services, each service to be of three months' duration and each to be staffed by 1 chief surgeon or physician, 1 senior assistant and either 1 or 2 junior assistants. Consultants in the various medical and surgical sub-specialties will also be appointed. A fee or weekly salary will be paid visiting physicians in accordance with the type and extent of medical services performed.

Further information concerning the Soldiers' Home in Holyoke may be obtained from James F. Collins, M.D., medical director, Soldiers' Home, Holyoke, Massachusetts (Telephone: Holyoke 2-9475).

CORRESPONDENCE

SUBJECTS NEEDED FOR STUDY

To the Editor: A grant-in-aid from the United States Public Health Service has been received by the Department of Psychiatry and Neurology, Boston University School of Medicine, for a study of "The Role of the Psychologic Factors Related to the Menstrual Cycle and the Sexual Life of Women in the Production of Epileptic Seizures." This three-year study involves intensive parallel psychiatric and physiologic investigations that will be carried out at the Massachusetts Memorial Hospitals. Serving as consultants to the project are Dr. William Malamud, professor and chairman of the Department of Psychiatry and Neurology, and Dr. Benjamin Tenney, Jr., professor and chairman of the Department of Obstetrics and Gynecology, both of Boston University School of Medicine, and Dr. Henry A. Murray, professor of clinical psychology at Harvard Medical School. The patients to be studied must be epileptic women between the menarche and the menopause who live in or near Boston, speak English, are not feebleminded, psychotic or alcoholic and do not have psychopathic personalities. The total number of such patients to be studied is necessarily limited, but we would very much appreciate referrals by any physician. Referrals may be made to either of the undersigned at 80 East Concord Street, Boston.

BERNARD BANDLER, M.D.
I. CHARLES KAUFMAN, M.D.

Boston, Massachusetts

POWERS OF TRUSTEES

To the Editor: In the June 28, 1951, issue of the *New England Journal of Medicine* the editorial "Hospital and Professional Relations" contains a statement that "there is no question that the lay trustees of a privately endowed hospital have the legal power to name the physicians who may use the facilities of the institution and to deny its use to any physician at their discretion."

I should like to inquire whether this is necessarily a true statement. It has been our impression that such a situation is so only in the event that the articles of incorporation or the constitution (or whatever the similar basic document of the corporation is called in a particular state) does not specifically provide otherwise.

This question has arisen in Ohio; we found, on advice of counsel, that the powers and duties of the lay trustees of a hospital are sharply limited by the articles of incorporation of the institution, which may or may not give the trustees the power to designate the physicians who may use the facilities of the institution.

I would very much appreciate knowing whether the statement in question was based on a legal opinion. The reason for this inquiry is that such flat statements are being iterated and reiterated with increasing frequency throughout the country — often without due consideration of their ultimate effect.

R. J. WHITACRE, M.D.
President of Medical Staff

Huron Road Hospital
Cleveland, Ohio

Note: The statement that Dr. Whitacre questions was not based on legal opinion. It was made as a starting point for the subsequent discussion. As such, perhaps it might better have been phrased: "Let it be assumed that the lay trustees of a privately endowed hospital have the legal power, and so forth." It seems entirely reasonable to suppose that the trustees have no such power if the articles of incorporation of an institution specifically deny it to them.

The interest aroused by the editorial emphasizes the desirability of clarification. Both the staff and the trustees of every hospital might well look into the legal constitution of their organization. This will vary from one hospital to another, and may well vary in different states. The situation that inspired the editorial was that a medical society had been called on by certain physicians to adjudicate such an issue. It seemed proper to point out that unless the medical society had been invited by both parties to a dispute to act as mediator, there was no compelling reason for it to act in such a capacity. — ED.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Biological Antioxidants: Transactions of the fourth conference, December 8–9, 1949, New York, New York. Edited by Cosmo G. Mackenzie, Department of Biochemistry, University of Colorado School of Medicine. Associate editors: E. V. Jensen, departments of Surgery and Chemistry, University of Chicago School of Medicine, and Ralph T. Holman, Department of Biochemistry and Nutrition, Agricultural and Mechanical College of Texas. 8°, paper, 181 pp., with illustrations. New York: Josiah Macy, Jr., Foundation, 1950. $3.25.

This conference was attended by fourteen members and nine guests. Eight articles on the biochemistry of oxidation and on various antioxidants were read and discussed.

Blood Clotting and Allied Problems: Transactions of the third conference, January 23–24, 1950, New York, New York. Edited by Joseph E. Flynn, Department of Pathology, College of Physicians and Surgeons, Columbia University.

8°, cloth, 224 pp., with 52 illustrations and 32 tables. New York: Josiah Macy, Jr., Foundation, 1950. $3.00.

The conference was participated in by sixteen members and eight guests. Fifteen articles on the various anticoagulants and on blood clotting in general make up the text. The publishing is excellent and the book should be in all collections on the subject.

Trends in Gerontology. By Nathan W. Shock, chief, section on gerontology, National Heart Institute, National Institutes of Health, and the Baltimore City Hospitals. 8°, cloth, 153 pp., with 12 illustrations. Stanford, California: Stanford University Press, 1951. $2.50.

This small monograph has been written as a companion to the author's large bibliography. It deals with the phenomena of aging in relation to community problems and research. The author advocates the establishment of an institute of gerontology. There are indexes of authors and subjects, and the publication is excellent. The book should be in all collections on the subject.

A Classified Bibliography of Gerontology and Geriatrics. (Prepared for Stanford University under a grant from The Forest Park Foundation, Peoria, Illinois.) By Nathan W. Shock, chief, section on gerontology, National Heart Institute, National Institutes of Health and the Baltimore City Hospitals. 4°, cloth, 599 pp. Stanford, California: Stanford University Press, 1951. $15.00.

This comprehensive bibliography on aging and the hygiene and disorders of old age is recommended for all medical libraries as a standard reference work. Likewise, it should be in all private collections on the subjects. There is a list of authors, and the publishing is excellent.

Amino Acids and Proteins: Theory, methods, application. Compiled and edited by David M. Greenberg, Ph.D., professor of biochemistry and chairman of the division, University of California School of Medicine, Berkeley, California. 4°, cloth, 950 pp., with illustrations and tables. Springfield, Illinois: Charles C Thomas, 1951. $15.00.

This composite book is the joint work of eighteen contributors. Each chapter has appended a select list of references. The publishing is excellent, and the book is recommended for all medical libraries and for all collections on biochemistry.

Return to Life. By Lily MacLeod. 8°, cloth, 128 pp. Philadelphia: J. B. Lippincott Company, 1951. $2.00.

In this popular book is told the story of a woman who was afflicted with cancer and in whom the disease has been arrested, and who hopes to return to a useful life.

Parasitic Infections in Man. Edited by Harry Most, M.D. Symposium held at the New York Academy of Medicine, March 15 and 16, 1949. 8°, cloth, 229 pp., with tables. New York: Columbia University Press, 1951. $4.50. Symposia of the section on microbiology, the New York Academy of Medicine: Number 4, Parasitic Infections in Man.

This symposium was conducted by the section on microbiology of the New York Academy of Medicine and fourteen specialists who discussed various aspects of parasitic diseases, with special emphasis on malaria, helminths and immunology of parasitic diseases. Lists of selected references are attached to each subject. The publishing is excellent except for the surprising lack of an index. The book is recommended for all collections on parasitology.

Nasal Sinuses: An anatomic and clinical consideration. By O. E. Van Alyea, M.D., associate clinical professor, Department of Laryngology, Rhinology, and Otology, University of Illinois College of Medicine, Chicago. Second edition. 8°, cloth, 327 pp., with 143 illustrations. Baltimore: The Williams and Wilkins Company, 1951. $9.00.

In this new edition the author has revised the text considerably, especially the clinical sections, to discuss the antimicrobial treatments. Bibliographies are appended to the various chapters, and there are indexes of authors and subjects. The publishing is well done and the illustrations are excellent. The book should be in all medical libraries and in the collections of rhinologists.

Ambulance Anecdotes. By Temple Fay, M.D. With illustrations by "Marge." 12°, cloth, 142 pp. Springfield, Illinois: Charles C Thomas, 1950. $2.50.

This interesting, humorous story of the ambulance and the hospital is well told and deserves a place in the literature on the lighter side of medicine.

The Use of Pedicle Flaps of Skin in Plastic Surgery of the Head and Neck. By Gordon B. New, M.D., professor of plastic surgery, and John B. Erich, M.D., associate professor of plastic surgery, of the Graduate School, University of Minnesota, Minneapolis, and Section on Laryngology and Oral and Plastic Surgery, Mayo Clinic, Rochester, Minnesota. 8°, cloth, 104 pp., with 76 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $3.00. (Publication Number 56, American Lecture Series.)

This small monograph is well illustrated and very well printed. It should be in all collections on plastic surgery.

Diabetes Guide Book for the Physician. Prepared by the Committee on Education of the American Diabetes Association. 16°, paper, 79 pp. New York, New York: American Diabetes Association, Inc., 1950.

This authoritative guidebook for physicians furnishes a simple but complete survey of the diagnosis and treatment of diabetes. The small book has been prepared by the Committee on Education of the association.

The Practice of Sanitation. By Edward S. Hopkins, principal associate engineer, Bureau of Water Supply, Baltimore, Maryland, Lieutenant Colonel, Medical Service Corps (Sanitary Engineering Section), USAR, and instructor, McCoy College, Johns Hopkins University; and Francis B. Elder, engineering associate, American Public Health Association, and Colonel, Medical Service Corps (Sanitary Engineering Section), USAR. 8°, cloth, 423 pp., with 109 illustrations. Baltimore: The Williams and Wilkins Company, 1951. $7.50.

This textbook has been written by two prominent sanitary engineers as a guide for the training of physicians, nurses, sanitarians and students. It seeks to bring together in one volume the facts concerning present-day sanitation practice in the United States. The whole field of environmental sanitation is covered in fourteen chapters. Lists of references cited in the text are appended to the various chapters. There are indexes of authors and subjects, and the book is well published. It should be in all collections on the subject.

English–German Medical Dictionary. Compiled by F. S. Schoenewald, M.D. 8°, cloth, 242 pp. Philadelphia: The Blakiston Company, 1951. $6.00.

This new dictionary of medical terms from English into German should prove valuable to medical librarians and physicians, especially if used in connection with Lang.

In addition to the strictly medical terms there are a great many ordinary nonmedical words commonly used in medical writing. A second part, of Germ n into English, if published, would make the dictionary complete and invaluable and supersede the Lang, which is now out of date.

The book is well published and is recommended for public and medical libraries.

Hemodynamics in Failure of the Circulation. By W. B. Youmans, M.D., Ph.D., professor of physiology, Department of Physiology, University of Oregon Medical School, Portland, Oregon, and A. R. Huckins, M. S., M. D., research assistant, Department of Physiology, University of Oregon Medical School, Portland, Oregon. 8°, cloth, 71 pp., with 10 illustrations. Springfield, Illinois: Charles C Thomas, 1951. $2.75.

This monograph presents systematically the mechanisms by means of which left-ventricular failure may lead to an elevation of both pulmonary and systemic venous pressure. The prominent role of the kidney in various types of failure is also described, and the reasons for the inconsistency of the relation between systemic venous pressure and the status of the right ventricle are made clear.

Virus and Rickettsial Diseases. By S. P. Bedson, M.D., F.R.C.P., F.R.S., professor of bacteriology, London Hospital; A. W. Downie, D. Sc., M.D., professor of bacteriology, University of Liverpool; F. O. MacCallum, B. Sc., M.D., director, Virus Laboratory, Central Public Health Laboratory; and C. H. Stuart-Harris, M.D., F.R.C.P., professor of medicine, University of Sheffield. 8°, cloth, 333 pp., with 33 illustrations. Baltimore: The Williams and Wilkins Company, 1950. $5.50.

This composite work presents an up-to-date analysis of the literature of the various virus and rickettsial diseases. Bibliographies are appended to the various chapters and there is an index of subjects. An author index would be valuable in this type of book. The printing was done in Great Britain and the publishing is excellent. The book is recommended for reference purposes to all medical libraries.

Neurotic Counterfeit-Sex: Impotence, frigidity, "mechanical" and pseudosexuality, homosexuality. By Edmund Bergler, M.D. 8°, cloth, 360 pp. New York: Grune and Stratton, 1951. $5.50.

The author, using the psychiatric-psychoanalytic method, traces the disturbances of sex life in both sexes according to genetic principles. He designates neurotic sex as "counterfeit sex." The text is divided into two sections: impotence, including male homosexuality; and frigidity, including Lesbianism. Each part is followed by short chapters on therapeutic procedures and chances of therapy. A bibliography precedes the text and there is a good index.

Malignant Diseases of the Female Genital Tract. By Stanley Way, M.R.C.O.G., gynaecologist to the Newcastle Regional Cancer Organization and associate surgeon, Gynaecological Department, Royal Victoria Infirmary, Newcastle-on-Tyne. 8°, cloth, 279 pp., with 38 illustrations. Philadelphia: The Blakiston Company, 1951. $5.00.

Dr. Way, in this monograph, analyzes the pertinent literature on carcinoma, sarcoma and other malignant tumors of the female genital organs. There is a special chapter on pregnancy complicated by malignant tumors. Lists of references are appended to the various chapters, and there are indexes of authors and subjects. The illustrations, type and publishing in general are excellent. The printing was done in Great Britain. The book should be in all medical libraries as a reference source.

NOTICES

ANNOUNCEMENT

Dr. John C. Trakas announces the opening of an office for the practice of otolaryngology at 1269 Beacon Street, Brookline.

THE LOWELL INSTITUTE

The Lowell Institute announces a course of four lectures on Medical Education — A Concern of the People, by James Howard Means, M.D., Jackson Professor of Clinical Medicine, emeritus, Harvard Medical School, and consultant in medicine, Massachusetts Institute of Technology.

The lectures will be given in the hall of the Boston Public Library on Mondays and Thursdays at 5 p.m., beginning on Monday, December 3. Tickets may be obtained from the curator of the Lowell Institute, Boston Public Library.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY

The American Society for the Study of Sterility announces the opening of the 1952 contest for the most outstanding contribution on the subject of infertility and sterility. The winner will receive a cash award of $1000, and the essay will appear on the program of the 1952 meeting of the society. Essays submitted in this competition must be received not later than March 1, 1952. Full particulars concerning requirements of this competition may be obtained from the American Society for the Study of Sterility, 20 Magnolia Terrace, Springfield, Massachusetts.

MEDICAL RESEARCH FELLOWSHIPS

The Medical Fellowship Board of the National Research Council is now accepting applications for postdoctoral research fellowships for 1952-1953 under the following program.

There are two groups of fellowships in the medical sciences, one supported by the Rockefeller Foundation, the other by the Lilly Research Laboratories. They provide opportunity for training in research in all branches of medical science. The Rockefeller Fellowships are open to citizens of the United States or Canada, the Lilly Fellowships only to citizens of the United States. Fellows must hold the degree of M.D. or Ph.D. The awards are intended for recent graduates who, as a rule, are not more than thirty years of age.

Fellowships in tuberculosis are available under a grant from the National Tuberculosis Association. These awards are limited in number and are designed to promote the training and development of investigators in fields related to tuberculosis. They are open to citizens of the United States who are graduates of American schools and who, as a rule, are not more than thirty years of age. Preference will be given to applicants who have the degree of M.D. or Ph.D.; only in exceptional circumstances will a fellowship be awarded to an applicant who has neither of these degrees.

Fellows will be appointed at a meeting of the Medical Fellowship Board early in March, 1952. Applications for consideration at this meeting must be filed on or before December 15, 1951. Appointment may begin at any time determined by the Board. Further information about these fellowships may be obtained from the Secretary of the Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

EXAMINATION FOR PUBLIC HEALTH SERVICE MEDICAL OFFICERS

A competitive examination for appointment of medical officers to the Regular Corps of the United States Public Health Service will be held on February 5, 6 and 7, 1952. Examinations will be held at a number of points throughout the United States, located as centrally as possible in relation to the homes of candidates. Applications must be received *no later than January 2, 1952.*

Application forms and additional information may be obtained by writing to the Surgeon General, United States Public Health Service, Federal Security Agency, Washington 25, D. C., attention: Division of Commissioned Officers.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The tenth annual meeting of the American Academy of Dermatology and Syphilology will be held in Chicago at the Palmer House, December 8-13.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The interim session of the American College of Chest Physicians will be held at the Ambassador Hotel, Los Angeles, California, on December 2 and 3. On Sunday, December 2, a scientific session will be presented by the California chapter of the college, including round-table luncheon discussions and an x-ray conference. A banquet will be held in the evening. The Board of Regents of the American College of Chest Physicians will meet on Monday, December 3, as well as various councils and committees of the college.

SOCIETY MEETINGS AND CONFERENCES

November 7-19. Pan-Pacific Surgical Association. Page 820, issue of May 24.

November 8, 20 and 27. Boston City Hospital House Officers' Association. Page 669, issue of October 25.

November 9. Rocky Mountain Harvard Medical School Alumni Association. Page 548, issue of October 4.

November 9, 16, 23, and 30, December 7, 14, 21, and 28 and January 4. New England Deaconess Hospital Clinics. Page 548, issue of October 4.

November 10-28. The Springfield Hospital. Page 670, issue of October 25.

November 13. Harvard Medical Society. Page 710, issue of November 1.

November 13. American Federation for Clinical Research (Boston Chapter). Page 709, issue of November 1.

(*Notices concluded on page xxi*)

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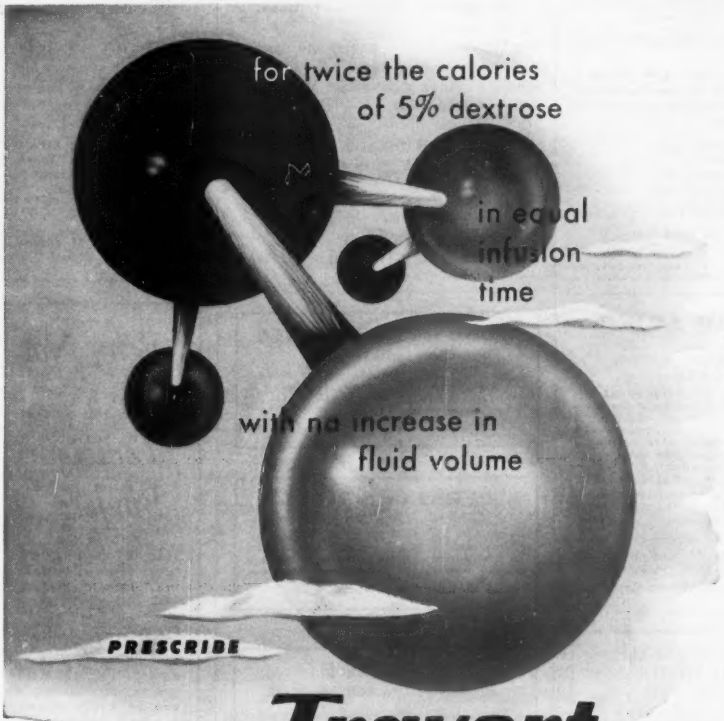

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NOTICES (*Concluded from page 752*)

NOVEMBER 13. New England Society of Anesthesiologists. Page 709, issue of November 1.
NOVEMBER 13. Springfield Academy of Medicine. Page 548, issue of October 4.
NOVEMBER 14. Salmon Memorial Lecture. Page 548, issue of October 4.
NOVEMBER 14. Northeastern New York Radiological Society. University Club, Albany, New York.
NOVEMBER 14 AND 15. Diabetes Fair. New England Diabetes Association. Page 669, issue of October 25.
NOVEMBER 18. Council of New England State Medical Societies. Page 709, issue of November 1.
NOVEMBER 19 AND 26. Beth Israel Hospital House Officers' Colloquium. Page 590, issue of October 11.
NOVEMBER 20. Salmon Memorial Lecture. Page 548, issue of October 4.
NOVEMBER 21. Alpha Omega Alpha Lecture. Page 669, issue of October 25.
NOVEMBER 27, JANUARY 22, FEBRUARY 26, MARCH 25 AND APRIL 24. Norfolk District Medical Society. Page 710, issue of November 1.
DECEMBER 2. American Academy of Dental Medicine. Page 548, issue of October 4.
DECEMBER 2 AND 3. American College of Chest Physicians. Page 752.
DECEMBER 5–8. New York State Society of Anesthesiologists. Page 710, issue of November 1.
DECEMBER 8–13. American Academy of Dermatology and Syphilology. Page 752.
DECEMBER 11–19. International Congress on Mental Health. Page xiii, issue of July 26.
DECEMBER 13. Pediatric Problems of the General Practitioner. Dr. James Marvin Baty. Pentucket Association of Physicians. 8:30 p.m. Haverhill.
DECEMBER 14 AND 15. Association for Research in Nervous and Mental Disease. Page 958, issue of June 21.
JANUARY 23, 1952. Suffolk District Medical Society. Page 669, issue of October 25.
MAY 1–3, 1952. American Goiter Association. St. Louis, Missouri.
JULY 8–11, 1952. Thirteenth British Congress of Obstetrics and Gynaecology. Page xv, issue of December 14.
JULY 14–19, 1952. International Congress of Physical Medicine. Page 998, issue of June 28.

DISTRICT MEDICAL SOCIETIES

HAMPSHIRE

JANUARY 2. Veterans Hospital, Northampton.
MARCH 5. Cooley-Dickinson Hospital, Northampton.
MAY 7. Annual Meeting. Jones Library, Amherst.

NORFOLK

NOVEMBER 27. Joslin Auditorium. New England Deaconess Hospital.
JANUARY 22. Veterans Administration Hospital, West Roxbury.
FEBRUARY 26. Boston Medical Library.
MARCH 25. Boston Medical Library.
APRIL 22. Boston Medical Library.
MAY 7. Place to be announced.

SUFFOLK

JANUARY 23. Massachusetts General Hospital.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 15

THURSDAY, NOVEMBER 15
*9:00–10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
*12:00 m.–1:00 p.m. Guest speaker. Stearns Auditorium, New England Center Hospital.
5:00 p.m. Case presentation and pathological discussion followed by a subject of special presentation. Joslin Amphitheatre, New England Deaconess Hospital.

FRIDAY, NOVEMBER 16
*8:15 a.m. Lipemia and Hypercholesterolemia and Diabetes. Drs. Higgins and Marble. Baker Clinic, New England Deaconess Hospital.
*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. New England Center Hospital.
*12:00 m.–1:00 p.m. Tumor Conference. Pratt Lecture Hall. New England Center Hospital.
*1:30 p.m. Tumor Clinic. Outpatient Department, Mount Auburn Hospital, Cambridge.

SUNDAY, NOVEMBER 18
2:00 p.m. Council of New England State Medical Societies. Copley Plaza Hotel.

MONDAY, NOVEMBER 19
*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street. Dr. Cleaveland Floyd in charge.
*12:00 m.–1:00 p.m. Endocrine Conference. Stearns Auditorium. New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheatre. Peter Bent Brigham Hospital.
2:00–8:30 p.m. Massachusetts Department of Mental Health Postgraduate Seminar in Neurology and Psychiatry. Metropolitan State Hospital, Waltham.
3:00 p.m. Gynecology Rounds. Mount Auburn Hospital, Cambridge.
*7:00–9:00 p.m. Combined Anesthesia Teaching Program of Boston. Stearns Auditorium, New England Center Hospital.
8:00 p.m. House Officers' Colloquium. Auditorium, Beth Israel Hospital.

TUESDAY, NOVEMBER 20
*12:00 m.–1:30 p.m. Surgical Grand Rounds. New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
7:00 p.m. Boston City Hospital House Officers' Association. New Cheever Amphitheatre. Dowling Building.

WEDNESDAY, NOVEMBER 21
*11:00 a.m.–12:00 m. Medical Clinic (Children's Medical Center). Amphitheatre, Children's Hospital.
*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Stearns Auditorium. New England Center Hospital.
*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Medical Center). Amphitheatre, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Combined Clinic of All Services (Children's Medical Center). Amphitheatre, Children's Hospital.
*4:00 p.m. New England States Chapter of the American College of Chest Physicians and the Overholt Clinic. New England Deaconess Hospital.

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Index to Advertisers

	PAGE
ABC Pregnancy Tests Laboratory	xviii
American Hospital Supply Corp.	xix
Ames Company, Inc.	ii
Atlantic X-Ray Company, Inc.	xiii
Baldpate, Inc.	xx
Baxter Laboratories, Inc.	xix
Boston Medical Supply Company	xviii
Burgess and Leith	xiii
Burroughs, Wellcome and Company	xii
Ciba Pharmaceutical Products, Inc.	iii
Commercial Solvents Corp.	viii
Crosbie–Macdonald	xiii
David Memorial Nursing Home	xx
Davies, Rose & Company, Ltd.	xvi
Electroencephalographic Laboratory, Inc.	xviii
General Electric Co., X-Ray Dept.	ix
Glenside, Inc.	xx
J. E. Hanger, Incorporated	xvii
Institute for Speech Correction, Inc.	xx
Kenmore Clinical Laboratory, Inc.	xviii
Kenmore Pharmacal Company	xiii
Leary Laboratory	xviii
Lederle Laboratories	iv
Eli Lilly and Company	Front Cover
Mead Johnson and Company	Back Cover
Medical Clearing Bureau, Inc.	xvii
Merck and Company, Inc.	xv
Perkins School	xx
R. J. Reynolds Tobacco Company	vii
Ring Sanatorium	xx
A. H. Robins Company, Inc.	after viii
Sears, Roebuck and Co.	xvii
E. R. Squibb & Sons	x, xi
The Upjohn Company	vi
Washingtonian Hospital	xvii
Westwood Lodge, Inc.	xx
Winthrop–Stearns, Inc.	xiv
Wiswall Sanatorium	xx
Woodside Cottages, Inc.	xx
Wyeth, Inc.	v

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